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CHRONIC PROLIFERATIVE OSTEOMYELITIS OF THE SKULL

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Chronic proliferative osteomyelitis, sclerosing osteitis, or osteoperiostitis may be demonstrated in some degree in every case of chronic inflammation within pneumatized bone. Radiographically this new bone formation is evidenced by increased density at the periphery of chronically infected sinuses. This condition represents bone regeneration due to stimulation of the osteogenetic tissues. Occasionally this process of bone regeneration proceeds until tumor formation or pressure symptoms bring the case above the clinical horizon.

Although osteomyelitis of the skull has received considerable attention in recent years, most reports deal with acute fulminating destructive infections in the calvarium in which there has been little time for the natural reparative processes to become manifest.

By definition, osteomyelitis is an inflammation of the bone and marrow spaces. The acute phase is characterized by exudation of cells, usually polymorphonuclear leukocytes, into the marrow spaces, and destruction of bone by osteoclastic activity. The beginning of

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the reparative process in the subacute phase is evidenced by angioblastic and fibroblastic proliferation in the marrow spaces. If this natural reparative process continues, a chronic stage of the infection is reached in which adult fibrous connective tissue develops in the marrow spaces and irregular masses or cords of new bone are produced by osteoblastic activity. All three of these phases of infection may be present in different sections of one osteomyelitic lesion. Thus, edema, purulency, and sequestrum formation may be demonstrated in one area, while fibrosis and involucrum formation may be present in another.

If in the healing process of osteomyelitis the fibroblastic and angioblastic proliferation is overabundant, this exuberant tissue results in excessive new bone formation which in some instances demonstrates a pattern like that of parent granulation tissue. This mass of new bone may be localized and atypically placed so that it simulates an osteoma or true bone neoplasm. Such bony excrescences should not be designated as osteomata since their growth depends upon continued chronic inflammation with the production of more and more granulation tissue; while a true osteoma or bone neoplasm continues to grow in the absence of any known exciting factor. These atypical masses of new bone represent chronic proliferative osteomyelitis with formation of osteomatoid excrescences. Of course it is conceivable that a true bone tumor might be produced by the irritation incident to chronic osteomyelitis.[1] Trauma likewise may produce the stimulus necessary for bone growth as noted in cases of hyperostosis and periostitis following injury.

This report is based upon a series of cases of proliferative osseous lesions of the skull in which infection may have been an important etiological factor. It is realized that the pathogenicity of such lesions may remain obscure even after exhaustive clinical and histopathological studies. However, the cases to be considered seem sufficiently important to justify investigation particularly in regard to possible inciting causes.

A review of the literature impresses upon one the fact that there is no unanimity of opinion regarding the pathogenesis of benign osseous tumors, and even leaves one confused in attempting to establish criteria for the histopathological diagnosis of these lesions.

Smith[2] quoted Ewing in stating that "circumscribed overgrowth of bone occurs under such a wide variety of conditions, and the distinctions between inflammatory and neoplastic hyperplasia of

the tissue are so often obscured that it has never been possible to exactly define the limits of osteoma".

Lang[3] attributes osteitis fibrosa cystica to trauma and irritation. He contends that the structure of the circulatory system in bone allows only slight compensation for circulatory disturbances. Hemorrhage into the bone marrow leads to bone resorption and cyst formation which in turn stimulates the production of new bone.

Davis[4] discusses chronic hyperplasia or focal osteitis fibrosa of the superior maxilla. He attempts to differentiate this lesion from osteoma or fibroma and states that focal osteitis, leontiasis ossea, and osteitis deformans are all the same disease but the latter two are diffuse forms of osteitis fibrosa. In the focal cases there are no changes in the calcium or phosphorus content of the blood serum.

Smith,[2] in discussing osteomata of the nose and sinuses, stated that in his experience many of the osseous lesions that were distinguished as tumors from their gross appearance, could not be classified as true neoplasms on microscopic examination. He believes that some of the osteomata of the nose and sinuses belong to the fibrocystic group of bone diseases and represent essentially a process of healing or repair. He suggests the following sequence of events: "Trauma—giant cell tumor—bone cyst—osteitis fibrosa—osteoma." He concedes that many osteomata may be "true neoplasms and begin as such."

Fetissof[5] in discussing the pathogenesis of osteomata of the nasal accessory sinuses agrees with others that trauma and inflammatory processes in the sinuses may play the role of the "necessary exterior irritant" in the development of these tumors.

The sclerosing nonsuppurative osteomyelitis of Garre, which occurs chiefly in the tibia or the femur, exemplifies the proliferative tendency of osteogenetic tissues when stimulated by low-grade chronic infection. Although the diagnosis of this condition has been a controversial problem, the consensus of such observers as Wishner,[6] Jensen,[7] and Jones[8] seems to be that the proliferative lesion is produced primarily by the irritation of low-grade chronic infection; and Wishner[6] believes that it may be reactivated by trauma.

Phemister[9] describes silent foci of osteomyelitis in the long bones and compares them with the silent apical dental abscesses in the alveolus. He suggests that radiographic demonstrations of localized cortical thickenings and sclerosis of cancellous bone may be due to healed small foci of infection. Phemister[10] also stated "chronic

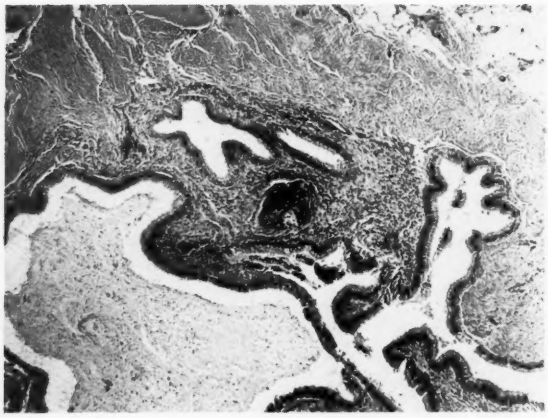

Fig. 1.—Photomicrograph of frontal sinus mucous membrane of dog transplanted to erector spinae muscle and removed for examination 13 months later. Pathological diagnosis:—"Living sinus mucosa. Small amount of new bone formation. Cyst formation. Slight foreign body reaction with an area of lipid-containing phagocytes."

fibrous osteomyelitis is a term that may be applied to any long-standing pyogenic infection of the bone in which the reaction on the part of the fibroblasts in contrast with the infiltrative cells becomes the outstanding feature of the lesion."

Thus in osteomyelitis, when mass necrosis is not produced, the usual picture of sequestrum and involucrum formation is lacking, and extensive formation of new bone may take place producing the picture of chronic proliferative osteomyelitis. This essential pathologic process may be found in either the long bones or in the skull. In the skull the proliferation of bone may take place on the surface or within the pneumatic spaces.

The proliferative tendency of any osteogenetic tissue is dependent upon the conditions of stimulation. The specificity of the periosteum and the osteoblasts has been questioned by Huggins,[11] who has shown that an altered environment may induce osteogenetic properties in certain other connective tissues. Phemister,[12] however, has stated that "most of the ordinary growth and repair of bone is accomplished by cells within and immediately on the surface of bone that have more ossifying tendency than the connective tissue cells outside of bone."

The pneumatic spaces of the skull are lined by mucoperiosteum which under conditions of functional stimulation is just as capable of forming new bone as is the external periosteum of the skull, the dura, or the periosteum of a long bone. In experimental studies on dogs it may be demonstrated (Fig. 1) that transplanting of frontal sinus mucous membrane into distant connective tissues will result in the formation of mucus retention cysts and the production of new bone. In the case cited the newly formed bone was demonstrated after one year. In other specimens removed and examined after a period of five months, the mucous retention cysts were demonstrated but no new bone was found.

Skillern[13] in 1936 reported five cases of obliterative frontal sinusitis and described the condition as a complication of chronic sinus disease. He concluded that chronic infection in the mucosa might spread to the bony walls of the sinus and produce osteomyelitis or osteogenesis depending upon the virulence of the infection and also to some extent upon the thickness of the layer of compact bone between the diploetic structure of the calvarium and the sinus cavity. He viewed the process of osteogenesis as an attempt to wall off the infection thus preventing spread to the diploe. In each of the cases in his report there had been some preceding intranasal operation. Coates[14] in discussing Skillern's paper said that he had seen some cases of obliterative frontal sinusitis after operations of the Lynch or Sewall type but that he had not noted the condition subsequent to minor operative procedures on the nose. He confirmed Skillern's opinion that the growth of new bone seemed to arise definitely from the anterior wall of the frontal sinus. Beck[15] reported a case in which x-ray evidence of obliteration of the frontal sinus occurred three months after a probe had been passed through the nasofrontal duct. Operation revealed a new growth of bone which simulated an osteoma.

The histologic picture of chronic proliferative osteomyelitis depends upon the stage of its development and the completeness of healing. Osteoid and pyogenic granulation tissue may be present, or normal appearing bone trabeculae with only fibrosis of the marrow spaces may predominate the picture. Thus, since there may be little or no evidence of the inflammatory nature of the process after complete healing, the problem of histopathologic diagnosis may be very difficult. In the cases to be presented it will be noted that the histologic picture is essentially the same in some instances where there is apparently a definite association with chronic suppuration as it is

in others which are associated with trauma but show no evidence of infection.

The diagnosis of chronic proliferative osteomyelitis must depend upon a combination of the clinical, radiographic, and histopathologic findings. It is quite possible that some of the so-called osteomata of the paranasal sinuses represent the result of continued osteogenesis from a small focus of chronic proliferative osteomyelitis on one of the walls of the involved sinus.

In the differential diagnosis of any osseous tumor of the skull, one will do well to keep in mind a classification of bone neoplasms and lesions simulating them. Meyerding[16] has published one in which there is a concise listing of the various bone neoplasms and the inflammatory, metabolic, and nutritional disorders of bone which may simulate them. Osteoma, hyperostosis, osteofibroma, osteitis fibrosa cystica, eburnated meningioma, and Paget's disease present the main problems of differential diagnosis in a case of chronic proliferative osteomyelitis of the skull. A positive diagnosis of a localized lesion is often impossible. The thickened sclerotic bone in and around the sinuses as seen in the roentgenograms may represent any of the above conditions. Occasionally one has the opportunity to observe the gradual obliteration of a sinus in serial films in a case of chronic suppurative sinus disease (Case 1, Fig. 2). The opportunity for clinical diagnosis of chronic proliferative osteomyelitis is found in those rare instances in which the new bone formation has progressed to tumor formation giving either external deformity or pressure symptoms.

REPORT OF CASES

Cases 1, 2 and 3 present the typical clinical picture of chronic proliferative osteomyelitis associated with a long standing chronic suppuration in the nasal accessory sinuses.

Case 4 presents the histopathologic picture of chronic proliferative osteomyelitis. However, the radiographic findings at the time of the patient's admission to the hospital before the drainage of the brain abscess and prior to the development of the recurrent scalp abscesses, suggest the possibility that this lesion represents a secondarily infected fibro-osteoma.

CASE 1.—K. G., male, aged 18 (Otology No. 352537). This patient was admitted to University Hospital on January 20, 1935, complaining of a head cold of five days' duration and swelling of the

Fig. 2. Case 1.—Roentgenograms made in January 1935 and April 1939.

left eye for two days. Examination revealed an acute purulent pansinusitis and a left orbital cellulitis. A left orbital abscess was incised and drained on January 22. The condition gradually improved although there was a small amount of purulent nasal discharge and slight proptosis by March 9. A recurrent orbital abscess was drained on June 8. By July 9, the infection had apparently subsided; there was no purulent discharge from the nose and no proptosis. X-ray films taken at this time demonstrated clouding of all paranasal sinuses.

The patient was readmitted to the hospital on April 13, 1939, at which time there was purulent drainage from the old incision near the inner canthus of the left eye. He stated that there had been continued drainage from this area for the preceding 17 months. Pus and polypoid hyperplasia were noted in the left middle meatus of the nose. X-ray films of the paranasal sinuses demonstrated a left frontal sinus that was considerably smaller than it had been at the time the previous x-ray films were made in 1935. The left frontal sinus appeared to be partially occluded by new bone.

A radical external frontal and ethmoid operation was done on April 15, 1939, at which time there was evidence of bone proliferation and partial obliteration of the left frontal sinus. The patholog-

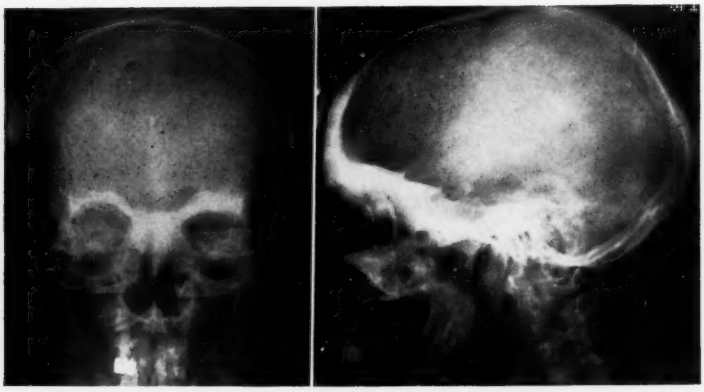

Fig. 3. Case 2.—Roentgenograms.

ical report was as follows: "Regeneration of bone in the frontal sinus, small fragment of bone and a little vascular granulation tissue and young scar tissue." Another specimen showed: "Chronic productive osteomyelitis of the frontal bone. Chronic purulent sinusitis in the soft tissue from the ethmoid sinuses."

CASE 2.—J. K., male, aged 50 (Otology No. 371205). This patient was admitted to University Hospital on October 22, 1935, complaining of pain in his right frontal area and attacks of unconsciousness. He stated that he had had "sinus trouble" for years. Six years previously an external operation had been done on the frontal and ethmoid sinuses on the right side. The patient had continued to have thick, yellow nasal discharge.

Examination revealed a scar in the right eyebrow. There was proptosis of the right eye and lag of the right upper eyelid. Polypoid degeneration of the right inferior turbinate was noted. The right middle turbinate had been removed. Polypoid mucous membrane and purulent discharge were seen in the region of the right nasofrontal duct.

Roentgenograms demonstrated the defect in the anterior walls of the frontal sinuses, more marked on the right. There was evidence of dense sclerosis in the ethmoid region on each side and in the region of each antrum.

Fig. 4. Case 3.—Roentgenograms.

On May 1, 1936, a bilateral external frontal sinus operation was done through a coronal incision. The frontal plate of the frontal bone was over ½ inch thick. The roof of the orbit which was also about ½ inch thick was removed nearly to the optic foramen.

Microscopic examination of excised tissue revealed thickened periosteum and irregular and thick bone trabeculae. Pyogenic granulation tissue was seen among bone fragments.

Case 3.—R. J. R., male, aged 48 (Otology No. 432876). This patient was admitted to University Hospital on October 24, 1938, complaining of thick, yellow nasal discharge associated with frontal headaches which had been present for about 25 years. About 20 years before admission to the hospital the patient had an intranasal operation on the left side. Five years later there was another intranasal operation, and during the four years prior to admission to the University Hospital, there were four more operations done upon the sinuses, of which three were intranasal and one was external.

Examination showed evidence of hyperplastic changes in the region of each middle meatus. There was a large amount of purulent discharge in each side of the nose, a draining fistula near the right inner canthus, and two small draining fistulas just beneath the brow on the left side.

X-ray examination demonstrated clouding of all the paranasal sinuses with an unusual degree of sclerosis in the frontal bone about both frontal sinuses.

On October 26, an external right frontal-ethmoid-sphenoid operation was done. The frontal sinuses were filled with pyogenic granulation tissue and pus. The sinus walls were greatly thickened apparently because of regenerated bone. The roof of the orbit was about 1 cm. thick and the intercellular septa in the ethmoids were thickened to the extent of 3-4 mm. The anterior wall of the antrum was also greatly thickened. The antrum was the seat of an empyema, and inside of this cavity there were three irregular bony masses covered with hyperplastic mucous membrane.

The pathological reports were: No. 1. "Marked hyperplasia of sinus mucosa showing extensive vascular proliferation and fibrosis. Chronic purulent sinusitis." No. 2. "Bony tissue, proliferating bone with fibrosis of marrow spaces and some necrosis of bone. Vascular pyogenic granulation tissue."

CASE 4.—D. F. G., female, aged 19 (Neurosurgery No. 216508). This patient was admitted to University Hospital on May 10, 1929, complaining of frontal headache, worse on the right side, which had been present for four weeks. She stated that during the preceding year she had had recurrent headaches. There had been three attacks, each lasting about a month, which were characterized by severe pain above the right eye. She said there was swelling of the right eye during the attacks.

On examination the patient was found to be acutely ill, irritable, and slightly confused. Temperature was 104° F. and the white blood cell count 18,000. X-ray studies of the skull demonstrated marked thickening of bone in the frontal region, suggesting a diffuse osteoma. Clinical diagnosis of right frontal brain abscess was made.

On May 29, a right frontal brain abscess was drained. The brain abscess was drained again on July 12.

The patient was again admitted to the hospital on May 26, 1931, complaining of headaches, and epileptic attacks which had been occurring about once a month for six months. She said that she had been in an automobile accident in January 1930, and sustained a skull fracture and scalp lacerations. The examination at this time revealed a right frontal scalp abscess. This was incised and drained. The abscess recurred and was incised and drained again on June 17.

On November 9, 1931, an operation was done for removal of a large area of thickened and infected frontal bone. The dura was covered with granulation tissue and there was a definite extradural

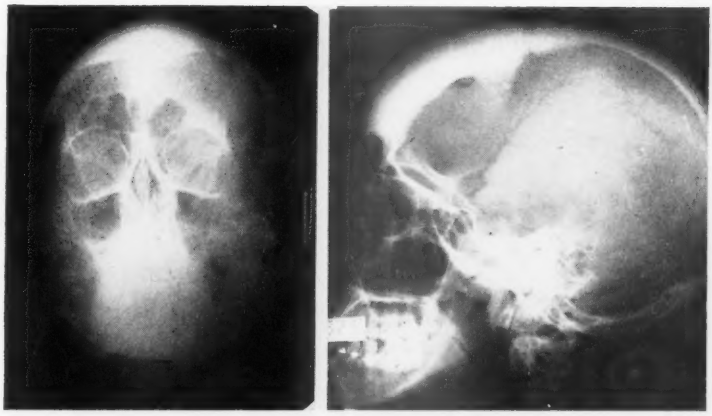

Fig. 5. Case 4.—Roentgenograms.

abscess. Grossly and clinically the thickening of the skull seemed to be typical of the so-called osteofibroma of the skull.

The pathological report was: "Chronic osteomyelitis with fibrosis of the marrow spaces."

Cases 5 and 6 demonstrate instances of bone proliferation in which infection might have played a part. In Case 5 there was no clinical evidence of suppuration in the frontal sinus but histopathologic studies revealed evidence of chronic productive inflammation. Clinically and radiographically the tumor appeared to be an osteoma. In Case 6 there was no gross pus in the mastoid but a mastoidectomy had been done presumably because of infection, and there was a small cholesteatoma in the mastoid process. The previous history of "exostoses" in the canal suggests the possibility that the lesion represented a recurrence of a benign osseous neoplasm, probably a fibro-osteoma.

Case 5.—V. K., male, aged 23 (Otology No. 349553). This patient was admitted to University Hospital on November 21, 1934, complaining of a mass over the left eye, which was first noted one year before this examination. There had been no pain and no associated respiratory infection. The mass had gradually become larger and the patient had developed diplopia.

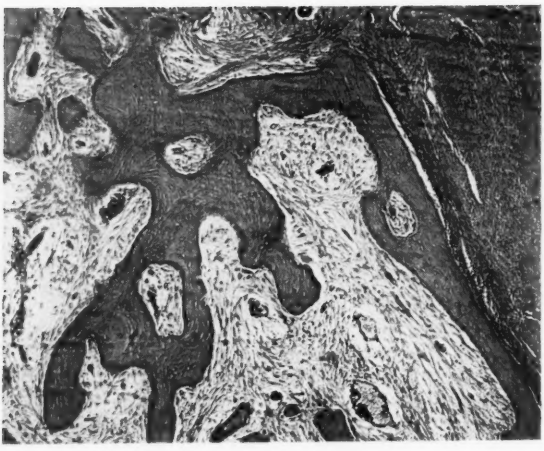

Fig. 6. Case 5.— Photomicrograph of excised tissue.

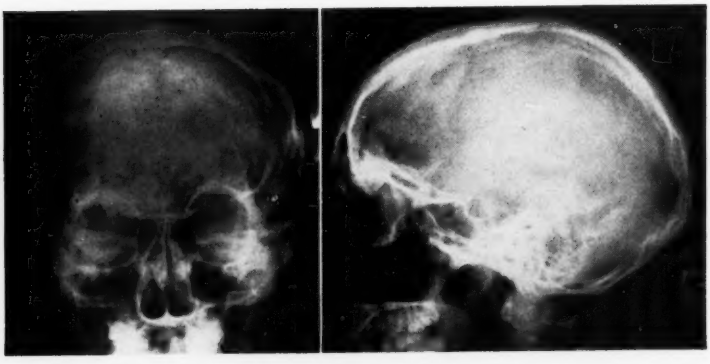

Fig. 7. Case 5.—Roentgenograms.

Examination demonstrated a bony hard intumescence in the left frontal region which obviously projected into the left orbit producing displacement of the globe. There was no clinical evidence of sinus suppuration. Radiographs demonstrated an irregular, apparently bony mass projecting into the superior portion of the anterior half of the left orbit and occupying the inferior two-thirds of the left frontal sinus.

At operation, a bony tumor was found protruding through the supraorbital ridge which apparently had been eroded by the tumor mass. The tumor was about 3 cm. in diameter and attached to the inner table of the frontal sinus by a sessile base. The tumor was removed. There was no evidence of pus in the sinus.

The pathological report was: "Sinus mucosa showing congestion and active chronic inflammation." "Bone from the region of the left frontal sinus shows chronic productive inflammation with new bone formation. Fibroblastic proliferation of the marrow spaces. Slight chronic sinusitis. No neoplasm."

CASE 6.—B. Z., male, aged 19 (Otology No. 455767). This patient was admitted to University Hospital on April 3, 1940, complaining of hearing impairment in the left ear, which had been present for seven years. Six years before admission to the hospital the patient had had a mastoidectomy and was told that there were "exostoses in the external canal." There had been a three year period of improved hearing after the mastoidectomy followed by gradual loss of hearing acuity.

Examination revealed a healed mastoid incision on the left. The external auditory canal was closed in the region of the isthmus by a bony hard mass covered by epithelium.

Radiographic studies demonstrated a small sclerotic mastoid. A left radical mastoidectomy was performed at which time the middle ear was found to be filled with bone. There was a small cholesteatoma in the posterior part of the mastoid which did not communicate with the tympanic antrum. The entire mastoid and middle ear, with the exception of that part of the mastoid occupied by the cholesteatoma, were filled with new bone. The malleus and the incus were embedded in regenerated bone which filled the external canal to the region of the isthmus.

The pathological report was as follows: "Compact bone with fibrosis of the marrow spaces, moderate proliferation of bone."

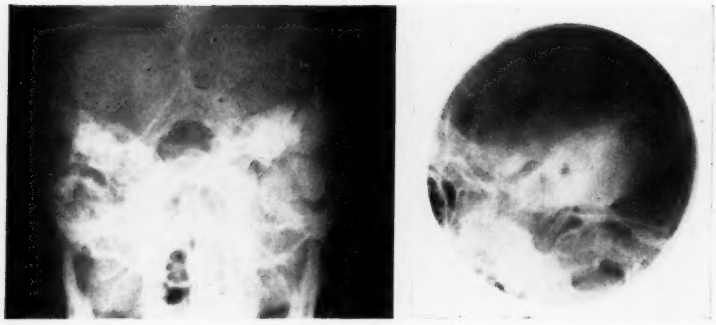

Fig. 8. Case 6.—Roentgenograms.

Cases 7 and 8 represent instances of bone proliferation subsequent to injury in which the pathological diagnosis of chronic proliferative osteomyelitis was made.

CASE 7.—E. S. H., female, aged 19 (Surgery No. 307033). This patient was admitted to the University Hospital January 23, 1933, complaining of pain in the left side of the forehead at the site of a small hard swelling. Three years previously, she had received an injury to this region in an automobile accident.

Examination revealed a small hard tumor in the left posterior frontal region which was not tender to pressure. There was no history or clinical evidence of sinus suppuration.

Roentgenograms demonstrated a lesion involving the left frontal bone at its midportion slightly anterior to the coronal suture. There was a rarefied central area about 1.5 cm. in diameter. Marked sclerosis of bone was noted at the periphery.

At operation, the intumescence was removed en masse and the dura was found to be normal.

The pathological report was as follows: "Very severe chronic periosteitis and osteomyelitis. Productive inflammatory changes with obliteration of marrow spaces. No tubercles. No neoplasm."

CASE 8.—A. J. G., male, aged 19 (Oral Surgery No. 447697). This patient was admitted to University Hospital on August 2, 1939, complaining of a swelling of the right side of his face and inability

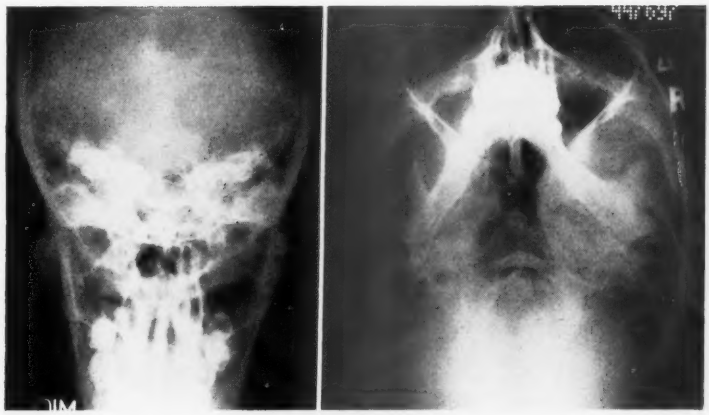

Fig. 9. Case 8.—Roentgenograms.

to open his mouth widely. There was a history of a blow on the chin six months previously which resulted in immediate swelling of the right side of the face with considerable pain and trismus. A fracture of the mandible was diagnosed at that time.

Examination demonstrated a deformity of the right side of the face consisting of a hard non-fluctuant, non-tender mass extending from the zygoma to the submaxillary region. The maximum swelling was in front of the lobe of the ear. There was moderate limitation of motion of the jaws.

Roentgenograms revealed marked enlargement of the right coronoid process and an increase in size of the ascending ramus of the mandible on the right. No evidence of fracture was noted. Roentgenograms taken six months later in February 1940 showed a definite increase in the lesion with sclerosis and overproduction of bone involving all structures adjacent to the right infratemporal fossa, and still later films in September 1940 showed evidence of continued progression of the lesion to involve the soft tissues at the base of the skull.

Operation consisted of taking a specimen for biopsy from the region of the coronoid process which, on pathological examination, demonstrated "proliferation of bone and absorption of bone. Fibrosis of marrow spaces. Chronic proliferative osteomyelitis."

Fig. 10. Case 9.—Roentgenograms.

This lesion was deemed inoperable because of its extensive invasion of the floor of the temporal fossa and the region of the petrous apex producing signs of irritation of the fifth and sixth cranial nerves.

Cases 9, 10, 11, and 12 represent a type of proliferative bone disease which must be classified histopathologically as fibro-osteoma. Since these reported cases were selected from a larger series recorded at the Univrsity of Michigan Hospital, one is impressed by the fact that the frontal bone is a not uncommon site of development of this lesion. From its clinical and gross pathological characteristics, the lesion is probably a true bone neoplasm.

Case 9.—M. G., female, aged 51 (Otology No. 504382). This patient was admitted to the hospital on May 29, 1942 complaining of headaches of increasing severity. The headaches which had been present for about six months were described by the patient as beginning in the teeth and radiating up over the top of the head to the occipital region, and gradually involving the entire head. She had noticed broadening of the nose and displacement of the left eye for about one month. Examination demonstrated a very broad nasal bridge with marked thickening of the bone in the region of the inner canthus of each eye, but more marked on the left. There was tremendous enlargement of the left middle turbinate, producing dis-

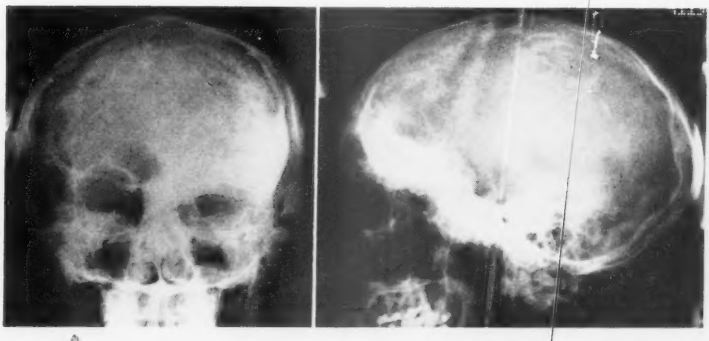

Fig. 11. Case 10.—Roentgenograms.

placement of the nasal septum to the right. No pus was seen in the nose.

Roentgenograms demonstrated proliferative and destructive changes of the frontal bone, more marked above and lateral to the left orbital region. Operation was done in two stages; first on June 3 the involved portion of the frontal bone was removed through a coronal incision. The dura showed no gross evidence of disease. The frontal sinuses were completely filled with cancellous bone. On June 22 an external ethmoidectomy was performed and it was found that the entire left ethmoidal labyrinth was filled with new bone. The greatly enlarged middle turbinate was removed. The lesion had the gross appearance of a tumor as it invaded and partially filled the sphenoid sinus.

The pathological report was: "Fine spicules of bone in large mass of dense fibrous connective tissue. No evidence of active inflammation. Lesion an ossifying fibroma which is moderately vascular."

Case 10.—C. L. R., male, aged 33 (Neurosurgery No. 411982). This patient ws admitted to University Hospital on October 20, 1937, complaining of convulsions of two weeks' duration. There was no history of sinus disease but there was a history of trauma of questionable significance in that the patient stated that he was hit on the head with a baseball bat at the age of five.

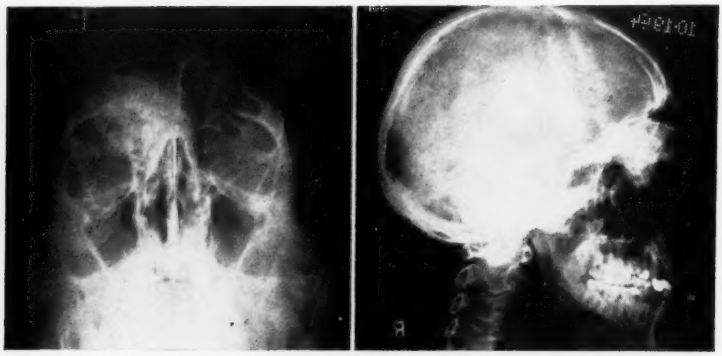

Fig. 12. Case 11.—Roentgenograms.

Clinical examination revealed a left proptosis and radiographic studies demonstrated extensive sclerosis of the frontal bone and obliteration of the left frontal sinus.

At operation, extreme thickening of the frontal plate of the frontal bone was found. The bony proliferation extended posteriorly in the orbit to the optic foramen where it had compressed the optic nerve.

The pathological report was as follows: "Dense bone with fibrosis of the marrow spaces. No evidence of active inflammation."

Case 11.—F. L., male, aged 27 (Otology No. 557726). This patient was admitted to University Hospital on October 22, 1944, complaining of a large mass above the right eye. He stated that at the age of eleven he was struck in the right eye with a baseball and about a year later he noticed a small swelling above the right eye which gradually increased in size without other symptoms except displacement of the eye. The patient thought that the tumor mass had grown somewhat more rapidly in the past seven years since a head injury which he was told was a right frontal skull fracture. Examination revealed a hard non-tender tumor mass above the right eye. There was displacement of the globe downward and forward. There was no clinical evidence of sinus infection.

X-ray studies of the skull demonstrated a large dense lesion which appeared to be neoplastic and which invaded the right frontal sinus and the right orbit.

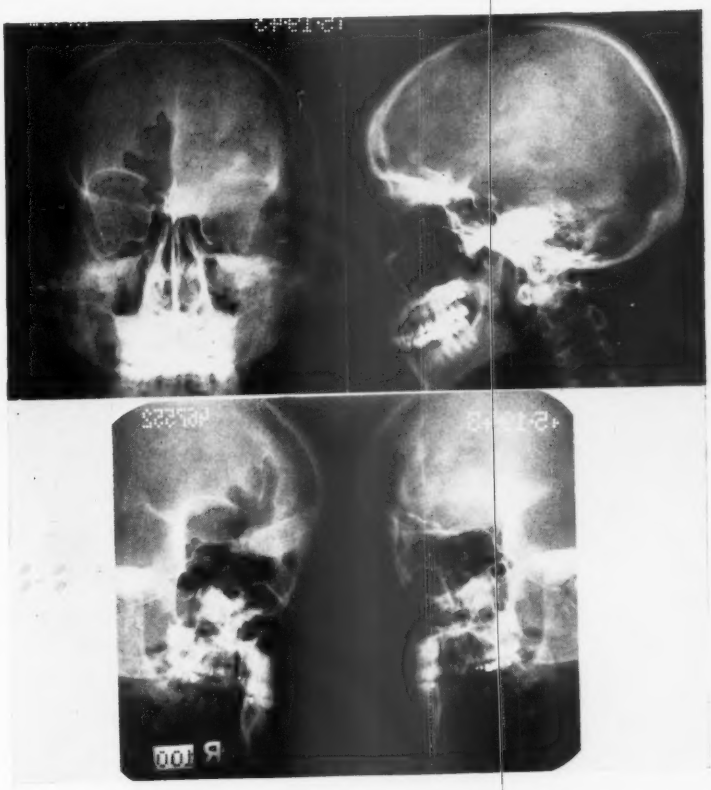

Fig. 13. Case 12.—Roentgenogram.

An external frontal operation was done on October 23. The right frontal sinus was found to be filled by a rather soft mass of bony tissue which could be removed with a curet. The lesion involved all of the orbito-ethmoid, the anterior, and the middle ethmoid cells. The roof of the orbit was involved nearly to its apex.

Pathological examination revealed what appeared to be spheres of lime salt in fibrous tissue, suggesting an ossifying fibroma. The sinus mucous membrane showed severe chronic mucopurulent inflammation. The mucous membrane was polypoid and contained numerous eosinophiles in the stroma.

CASE 12.—L. K., female, aged 29 (Otology No. 467552). This patient was admitted to University Hospital on May 18, 1943, complaining of protrusion of the left eye. The left proptosis had developed gradually over the preceding three years. There was some associated pain deep in the left orbit and an occasional lancinating pain in both temporal areas, worse on the left than on the right.

Examination revealed forward and slightly downward proptosis of the left eye. No mass was palpable in the orbit, but there was marked thickening of the supraorbital ridge. No evidence of sinus infection was found.

X-ray studies demonstrated a marked thickening and increased density of bone in the roof of the left orbit and in the supraorbital ridge. The abnormal bone appeared to end rather abruptly at the level of the upper border of the left sphenoid bone and did not cross the midline to involve the right frontal sinus.

Operation was performed October 7, 1943. Through a coronal incision the thickened abnormal portion of the left frontal bone was removed. The frontal bone was about 2 cm. thick in its vertical portion. The roof of the orbit was tremendously thickened to the extent of about 2 cm. The bone had the gross appearance of a so-called osteofibroma, and the lesion ended abruptly in the midline of the frontal region. The left frontal sinus was obliterated by the new bone formation, and the anterior ethmoids were partially filled by the tumor. The greatly thickened roof of the orbit was removed and the optic nerve was decompressed. The bone over the optic nerve was nearly 1 cm. in thickness.

The pathological report was that of an ossifying fibroma, apparently a true bone neoplasm. In one small area active purulent inflammation in the marrow spaces was noted, but this was interpreted as being of secondary importance.

Fig. 14. Case 13.—Roentgenogram.

CASE 13.—S. T., female, aged 10 (Otology No. 276009). This case is similar to the preceding cases in that a diagnosis of fibro-osteoma was made. The history of trauma is of particular interest. This patient was admitted to University Hospital on October 8, 1931, complaining of swelling of the right cheek. Four months previously she had been struck on the right cheek by a baseball. The swelling which occurred immediately after this injury had persisted. There was no history of sinus suppuration.

Examination revealed a non-tender bony hard enlargement of the right maxilla. The right upper alveolus was considerably widened. There was no clinical evidence of sinus infection.

X-ray studies demonstrated diffuse increased density in the region of the right maxillary antrum.

Operation was performed on October 12. A rather soft, sugary bony mass was found involving the alveolus and filling the right antrum.

The pathological report indicated a benign neoplastic bone proliferation, showing atypical bone trabeculae with atypical fibrous connective tissue filling the small marrow spaces. The diagnosis of a fibro-osteoma was made.

SUMMARY

Chronic proliferative osteomyelitis of the skull is presented as a clinical and pathological entity. Its method of development from

functional stimulation by low-grade infection of osteogenetic tissues is discussed. Various opinions regarding the pathogenesis of proliferative bone lesions are recorded. The difficulties of differential histopathological diagnosis are considered, and some of the other proliferative bone lesions of similar histological architecture are enumerated.

The diagnosis of chronic proliferative osteomyelitis demands the correlation of the clinical, the radiographic, and the gross and microscopic pathological findings. Histopathological diagnosis is facilitated by preparing an ample specimen for microscopic study of various portions of the excised tissue.

In its early and active phase, chronic proliferative osteomyelitis may be confused with other chronic infectious granulomata. If the lesion is old, demonstrating mature fibrous connective tissue in the marrow spaces, it will show essentially the same characteristics as a hyperostosis of traumatic origin. This lack of evidence of active inflammatory response in older cases makes it difficult also to differentiate them from the lesions of osteitis fibrosa cystica, Schüller-Christian's disease and Paget's disease. In the latter instances, however, examination of an ample specimen will reveal evidence of marked osteoclastic activity while in cases of hyperostosis or healed chronic proliferative osteomyelitis the osteoblastic activity will be predominant. In cases of fibro-osteoma or ossifying fibroma the presence of atypical bone trabeculae and atypical fibrous connective tissue in the marrow spaces reveals what may be considered as their true neoplastic nature.

COMMENTS

Chronic proliferative osteomyelitis of the skull adjacent to the sinuses apparently represents osteogenesis resulting from functional stimulation of the osteogenetic properties of the mucoperiosteum. Occasionally the new formed bone continues to grow to tumor proportions and involve the skull beyond the bounds of the paranasal sinuses.

The factual data available do not allow a positive statement to be made regarding the factors which tend to stimulate the osteogenetic properties of the mucoperiosteal lining of the paranasal sinuses. Since many patients with chronic proliferative osteomyelitis and obliteration of the sinuses have undergone surgical operations for the relief of chronic sinus disease prior to the development of

the obliterative process, it would seem likely that surgical trauma in addition to a chronic low-grade infection may play a part in the development of this condition. Perhaps partial separation of the mucoperiosteum from the bony walls of the sinus is a factor in stimulating bone regeneration.

Treatment in the form of complete surgical removal of the newly formed bone is indicated when the disease has progressed to the point of producing pressure symptoms or the appearance of tumor.

I am indebted to Major Walter P. Work, A. U. S., for his assistance in the early stages of work incidental to the preparation of this paper. When Major Work was Instructor in Otolaryngology at the University of Michigan Medical School in 1941, he collaborated with me in a study of proliferative bone diseases. His assistance in reviewing the voluminous literature on the subject, and in the experimental work on dogs is deeply appreciated.

201 SOUTH MAIN STREET.

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LXVI

EFFECT OF PENICILLIN LOZENGES ON CLINICAL AND BACTERIOLOGICAL FINDINGS OF PATIENTS

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The value of local application of chemotherapeutic agents to the site of a potential infection, before such a process develops, has adequate support from considerations of the pathogenesis of the infectious processes as well as the results of actual clinical trials. After an infection has developed, the rationale for bringing the drug to the site of the advancing infectious process by way of the blood stream appears to be better than that for local administration of the chemotherapeutic agent.

Several reports on the local use of penicillin in oral and throat infections have been made. Among the first to investigate such therapy were MacGregor and Long.[1] Others have followed. They found it possible to reduce the number of organisms in the throat and mouth and often to produce sterile specimens. It seemed desirable to add additional evidence, clinical and bacteriological, to the findings already reported on this type of penicillin therapy.

Clinical Procedure. Two groups of patients were investigated. The first consisted of 26 patients, specimens from whom were examined bacteriologically during and after the period of therapy with penicillin lozenges. In this group were eleven cases of tonsillectomy, five tooth extractions, four normal controls, and six miscellaneous conditions of the mouth and throat.

The second group consisted of a larger number of patients having acute pharyngitis and acute tonsillitis who were followed by clinical observation alone.

Each lozenge contained 500 Oxford units of penicillin in a lactose base. The base consisted of 8.4 grains of lactose, 9.2 grains

of sucrose, and a trace (0.05 gr.) of magnesium stearate per tablet. The last two ingredients were used as granulating substances. A similar lozenge containing 1000 units of penicillin was used in some of the cases not examined bacteriologically.

Specimens for bacteriological examination were taken 24 hours preoperatively to determine the bacterial flora of the oral cavity prior to the use of the lozenges. The culture was obtained by first having the patient rinse his mouth, and then gargle with 20 cc. of 0.85 per cent sodium chloride solution. This washing was labelled by number only and sent to the laboratory. A similar specimen was taken shortly after the operation and prior to the use of lozenges.

Soon after the second washing was taken, the patient was given the penicillin lozenges. He was instructed to keep a lozenge in the mouth almost continuously during waking hours. The lozenge was retained in the lower gingivolabial groove without sucking or manipulation with the tongue. The lozenges were alternated from side to side throughout the day. The patient was requested to record the length of time each lozenge remained in the mouth. Subsequent cultures were taken every 24 hours and clinical observations made at that time.

Lozenges containing lactose only were used in two cases in an attempt to determine whether increased salivation simulated the effects of the penicillin lozenges bacteriologically and clinically.

Clinical Observations. In general the lozenges were well tolerated by most of the patients. A few considered the taste moderately unpleasant but none refused the medication. A mild degree of nausea without vomiting was noted by several patients.

One patient experienced discomfort, localized to his soft palate, and manifested an erythematous eruption in the same area, while using the lozenges. These signs and symptoms disappeared 48 hours after the cessation of medication. This was considered to be a local reaction to penicillin and was the only one noted in this study.

The retention of the lozenges in the oral cavity varied considerably in different patients. The shortest time reported was 15 minutes and the longest three hours. Careful control by the patient usually resulted in a persistence of the lozenge of approximately one and one-half hours. The majority of the patients used between eight and twelve lozenges daily, or a total of 4000-6000 units of penicillin per diem. Some of the clinical observations were made on patients receiving 1000-unit lozenges.

Evaluation of clinical results was difficult because of the necessity of depending on subjective impressions without clear-cut criteria. Moreover, the conditions for which the lozenges were used varied markedly. One must admit also that these studies were carried out at a time when penicillin was widely publicized as a valuable form of therapy and thus the effect of suggestion may account for some of the subjective improvement noted by the patients. However, it was interesting to observe that numerous members of the hospital staff requested penicillin lozenges during attacks of acute pharyngitis and reported beneficial results. In spite of the lack of objectivity in these observations there is suggestive evidence here of the beneficial action of penicillin used locally.

Patients using penicillin lozenges after tonsillectomy generally appeared to have less membrane in the tonsillar fossae than those not using the medication, and complained less of pain than control patients. Two patients using lactose lozenges without penicillin, after tonsillectomy, showed more evidence of infection and membrane formation than untreated patients. It is possible that the lactose encouraged the growth of bacteria. Patients using penicillin lozenges after dental extractions appeared to experience less postoperative pain and secondary infection than those not treated. Several cases of acute tonsillitis were treated with penicillin lozenges with no apparent benefit. There was a similar lack of improvement in cases of well-established severe pharyngitis. However, penicillin lozenges seemed to be of definite value in the treatment of early cases of pharyngitis. The patients thought that their symptoms were of shorter duration than in previous attacks of sore throats. One might suspect that topical penicillin is effective in superficial infections of the throat and that its value diminishes if the organisms have penetrated deeper into the tissues.

Penicillin lozenges were used with four patients having Vincent's angina. Definite symptomatic relief occurred with all of them, but unfortunately they were not followed long enough to permit a final conclusion.

Bacteriological Procedures. As previously indicated, the samples were received in the bacteriology laboratory labelled only with the sample number. All correlations with clinical procedures were made after a group of samples had been studied bacteriologically. One Ml. of the sample was placed in each of three tubes. To one tube, 2 Ml. of 0.85 per cent sodium chloride solution was added; to the second, 2 Ml. of solution of cysteine hydrochloride. Later, begin-

ning with sample No. 159, 2 Ml. of a 1 per cent solution of "clarase" was used as a penicillinase in place of the cysteine, as it was more effective. To the third tube was added 2 Ml. of a solution containing 200 units of penicillin, in order to determine the susceptibility of the flora of the sample to this agent. Beginning also with sample No. 159, a fourth tube was added containing the sample, additional penicillin and clarase as a further check on the clarase action on added penicillin in the specimen.

Plain, blood and chocolate agar were then spread with 0.1 cc. of appropriate dilutions of the sample. Twenty-four plates were made of each specimen. The number of the different types of colonies was estimated and a range of 10 to 15 types was noted. Finally, an estimation of the penicillin content of the specimen was made beginning with sample No. 156, using the disc method with staphylococcus aureus (P209) as the test organism.[2]

Bacteriological Findings. Table I presents data from 6 of the 26 patients (175 samples) studied. The cases selected for presentation are typical. It was deemed desirable to present only data pertaining to total and streptococcus viridans counts. These included samples treated in the various ways, and inoculated on different media as described. It will be noted from the results presented in Table I that:

1. This type of therapy had no effect on the total count of some samples, but in others it showed a decrease from tenfold to a hundredfold (column 6).

2. Streptococcus viridans was practically eliminated from the oral and throat flora of 14 of the 26 patients studied. Because of insufficient data it was not possible to confirm indications of similar effects in 5 other patients. Three showed no change in the streptococcus viridans flora, and in these cases the organism was penicillin-resistant.

3. The addition of cysteine, which was discontinued in favor of clarase after sample No. 159, appeared to decrease streptococcus viridans rather than increase it by removing the penicillin.

4. The penicillin content of 119 samples tested was determined to be 0 in 108 samples and varied from 0.06 units to 5.0 units in the other 11 samples. It is probable that the standard technique used for this assay is not sensitive enough to detect amounts of penicillin which may be therapeutically significant.

Besides the data obtained in the study of specimens from patients, certain findings were made in laboratory experiments. One subject from the laboratory, W.E.C., was found to harbor a streptococcus hemolyticus. The effect of penicillin lozenges on both the streptococcus hemolyticus and viridans flora of this subject is indicated in Tables II and III. It will be noted that the flora was rapidly reestablished once penicillin lozenge therapy was stopped.

A few additional findings resulting from laboratory experiments are herewith listed:

1. Persistence of penicillin in the mouth was studied. It was noted that it could not as a rule be demonstrated ten minutes after the disappearance of the lozenge. This was also the case when five lozenges were taken in succession within one hour.

2. The persistence of penicillin could be increased by minimizing swallowing.

3. Penicillin activity is slightly lowered by the presence of mouth washings.

4. Several of the samples of mouth washings in which the penicillin could be demonstrated were stored at 5° C. There was little or no loss of activity after 10 to 15 days.

5. The bacteriostatic rather than bactericidal effect of penicillin lozenges on streptococcus hemolyticus in the oral flora of W.E.C. was demonstrated by adding clarase and obtaining counts of this organism of the same magnitude as were obtained before the penicillin lozenge therapy.

SUMMARY

The clinical findings made in this study indicate that patients given penicillin lozenges after tonsillectomy appeared to have less membrane formation in the tonsillar fossae. They also complained less of pain than patients not so treated. Similar findings were made in patients following dental extractions. Penicillin lozenge therapy seemed to be of little value in deep-seated tonsillitis or pharyngitis but appeared to have definite value in early cases of pharyngitis.

Bacteriological findings support the clinical observations. The total, and more particularly the streptococcus viridans, counts of mouth and throat flora were lowered by penicillin lozenge therapy. The persistence of penicillin in mouth washings was of short duration after the disappearance of the lozenges.

It is probable that preoperative use of penicillin may significantly lower the degree of transient bacteremia, which may follow operations in an infected area. Thus it may decrease the small but nevertheless real incidence of complications which are associated with such procedures.

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TABLE I.

VARIATIONS IN TOTAL COUNT AND STREPTOCOCCUS VIRIDANS FLORA IN THREE REPRESENTATIVE PATIENTS.

				Bacteriology					
	Sample		Lozenges	Untreated Sample		Ratio of viridans in untreated and treated samples			
Patient	No.	Time	Penicillin	Total	Viridans	A/C	A/D	A/E	Penicillin Assay
T.J. (Tonsillectomy)									Units
	204	pre-op.	—	4(a)	4	4/4	4/4	4/4	0
	210	1st day							
	212	2nd day	+	3	0	0/0	0/2	0/3	0.1
	216	3rd day	+	5	5	5/0	5/0	5/0	0
	220	4th day	+	5	0	0/0	0/0	0/0	0
	226	5th day	+	5	0	0/0	0/0	0/0	0
	236	6th day	—	4	4	4/4	4/4	4/4	0
O.S. (Excision of Carcinoma of Tonsil)									
	190	1st day	—	4	4	4/3	4/4	4/4	0
	191	2nd day	+	3	0	0/0	0/0	0/0	0.4
	194	3rd day	+	5	5	5/5	5/5	5/5	0
M.P. (Stomatitis)									
	197			5	4	4/4	4/4	4/4	0
	199		+(1)b	5	4	5/4	4/4	4/4	0
	202		+(2)	5	5	5/5	5/5	5/5	0
	208		+(3)	5	4	4/4	4/4	4/4	0
	211		+(4)	5	4	4/4	4/4	4/4	0
	219		+(6)	No sample received					
	227		+(7)	4	4	4/4	4/4	4/4	0
	237		+(10)	5	4	4/4	4/4	4/4	0
	238		+(11)	4	4	4/4	4/4	4/4	0
	243		+(16)	5	5	5/5	5/5	5/5	0

(a) 1=10; 2=10-100; 3=100-1000; 4=1000-10,000; 5=10,000+ per ml.

(b) Indicates consecutive days on or off treatment at time sample was taken.

(c) A/C=Total viridans count A over viridans count C following addition of penicillinase.

(d) A/D=Total viridans count A over viridans count D following addition of penicillin.

(e) A/E=Total viridans count A over viridans count E following addition of penicillin and penicillinase.

TABLE II.

STREPTOCOCCUS HEMOLYTICUS IN MOUTH WASHINGS OF SUBJECT W.E.C. ON 14 CONSECUTIVE DAYS ON OR OFF PENICILLIN TREATMENT.

		Bacteriology				
	Lozenges	Untreated Sample		Ratio of Hemolyticus in Untreated and Treated Samples		
Sample	Penicillin	Total	Hemolyticus	A/C	A/D	A/E
81	—	5(a)	3	3/2	3/3	3/3
82	—	5	3	3/3	3/3	3/3
83	—	5	3	3/2	3/3	3/3
84	+	5	1	1/0	1/0	1/0
85	—	5	2	2/2	2/2	2/2
86	—	5	4	4/4	4/4	4/4
87	+	4	2	2/0	2/0	2/0
88	+	3	0	0/0	0/0	0/0
89	+	3	0	0/0	0/0	0/0
90	—	5	0	0/0	0/4	0/2
91	—	5	2	2/2	2/2	2/2
92	—	5	3	3/3	3/3	3/3
93	—	4	4	4/2	4/3	4/4
94	—	5	3	3/3	3/3	3/3

(a) 1=10; 2=10-100; 3=100-1000; 4=1000-10,000; 5=10,000+

TABLE III.

TOTAL BACTERIAL COUNT AND STREPTOCOCCUS VIRIDANS FLORA IN MOUTH WASHINGS OF SUBJECT W.E.C. ON 14 CONSECUTIVE DAYS ON OR OFF PENICILLIN TREATMENT.

		Bacteriology				
	Lozenges	Untreated Sample		Ratio of Viridans in Untreated and Treated Samples		
Sample	Penicillin	Total	Viridans	A/C	A/D	A/E
81	—	5(a)	4	4/4	4/4	4/4
82	—	5	4	4/4	4/4	4/4
83	—	5	4	4/4	4/4	4/4
84	+	5	3	3/3	3/3	3/0
85	—	5	4	4/4	4/4	4/4
86	—	5	4	4/4	4/4	4/4
87	+	4	4	4/3	4/4	4/4
88	+	5	0	0/0	0/0	0/0
89	+	3	0	0/0	0/0	0/0
90	—	5	4	4/4	4/4	4/4
91	—	5	4	4/4	4/4	4/4
92	—	5	4	4/4	4/4	4/4
93	—	4	4	4/4	4/4	4/4
94	—	5	4	4/4	4/4	4/4

(a) 1=10; 2=10-100; 3=100-1000; 4=1000-10,000; 5=10,000+

LXVII

TONSILLECTOMY IN EARLY CONVALESCENCE FROM ACUTE TONSILLITIS WITH THE PROPHYLACTIC USE OF SULFONAMIDES

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and

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It has been the definite policy of most surgeons and has become almost an unwritten rule in the Army Medical Corps, to avoid tonsillectomy in patients recently suffering from acute tonsillitis. Operation has been postponed for six weeks to three months after the subsidence of the acute attack. This caution was warranted as the result of former experiences with postoperative complications. In the past many patients have been seen with postoperative exacerbation of the preceding infection, which had become quiescent clinically but had not completely "burned out." Such complications manifest themselves principally by chills and fever, high postoperative temperature elevations, acute arthritis, acute nephritis and septicemia.

Because of this postponement of surgery a difficult situation arose in the Army. Many soldiers suffering from repeated attacks of acute tonsillitis have been denied the necessary surgery because of frequent change of station. We have seen patients who have had four or five admissions to different hospitals for acute tonsillitis during a period of 12 to 15 months, with the loss of two or three months' time from active duty because of repeated attacks of tonsillar infection.

After encountering this situation many times it was decided to select a series of patients with long histories of recurrent acute sore throat and operate on them a short time after their clinical recovery from an attack. The procedure decided upon was to give each patient a prophylactic course of sulfonamide just before, and for a period of time after operation.

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The patients selected for such treatment were those convalescent from acute follicular tonsillitis, acute Vincent's infection complicated by beta hemolytic streptococcus infection, and acute sore throats without exudate but with positive beta hemolytic streptococcus cultures. The first such case was operated on in October 1942.

Of the first 100 patients operated on, 50 per cent received sulfonamide therapy during the acute phase of the infection, when first admitted to the hospital, and 50 per cent were treated symptomatically without sulfonamide therapy during the acute phase. Tonsillectomy was performed in each case from two to five days after clinical recovery; that is, when the temperature had returned to normal, the local edema had disappeared, and the glands of the neck were no longer tender. In several of the patients suffering from Vincent's infection, there was still some exudate but spirochetes were not demonstrated in stained smears or by dark field examination. In 90 per cent of the 100 cases beta hemolytic streptococci were recovered at the time of admission to the hospital. Five patients had persisently positive cultures for beta hemolytic streptococci at the time of operation. Each patient received six grams of sulfadiazine or sulfathiazole during the 24 hours preceding surgery, and four grams daily for five days postoperatively. Both drugs appeared equally effective. In a small number of cases penicillin was used because of sulfonamide sensitivity. Good results were obtained in these cases also. All operations were performed under general anesthesia.

This group was compared with 100 elective tonsillectomies in which there was no evidence of acute tonsillar infection prior to operation. Of the two groups, the one receiving prophylactic sulfonamide therapy presented slightly lower postoperative temperature elevations. In no case did the temperature exceed 100.6° F. and in most instances the maximum elevation was 99.6°. According to the nurses' notes pain was less marked on swallowing, which resulted in improved fluid intake in the group receiving sulfonamides. Recovery was as rapid and healing as clean as in the elective cases and there was no greater incidence of postoperative bleeding. No patient in the treated group developed any serious complications. Since the time of the original comparative study 100 additional patients, most of whom were convalescent from acute tonsillitis, were operated on with the prophylactic use of sulfonamide drugs and recovery was uneventful.

SUMMARY AND CONCLUSIONS

It has always been considered advisable to postpone surgery of the tonsils for some weeks following subsidence of acute infection. The evidence presented, however, indicates that tonsillectomy may be performed with safety directly following initial recovery from acute follicular tonsillitis provided sulfonamide drugs are administered prophylactically during the 24 hours preceding and for five days following the operation.

In the present study 100 tonsillectomies were performed immediately following subsidence of acute tonsillitis with the prophylactic use of sulfonamide therapy. These cases were compared to 100 elective tonsillectomies in which no drug was administered. The postoperative course of those who received sulfonamides was in general better than that of the elective cases. One hundred additional patients, most of whom were convalescent from acute tonsillitis, were operated on with the routine use of prophylactic sulfonamide therapy and the postoperative course in those cases was uneventful. In a small number of patients where sensitivity to sulfonamides prevented the use of these drugs, penicillin was substituted, with equally good results.

In the Army where the frequent movement of troops has interfered with the final accomplishment of tonsillectomies after the usual rest period of six weeks following acute infection of the tonsils, the usefulness of early operation has been particularly apparent. The operation under the conditions described has not only been proven to be safe but has reduced days lost from active service. In addition it would appear that the hazard of more severe complications resulting from recurrent acute tonsillitis would be diminished by this procedure.

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LXVIII

MAXILLARY SINUS DRAINAGE

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The maxillary ostium in a healthy state is of ample size and the anatomic relations are such as to provide an adequate drainage outlet for the maxillary sinus.

In an acute sinusitis the immediate reaction to the invasion of pathogenic organisms results in a swelling of the tissues which constrict the lumen of the ostium to retard or block completely the discharge of pus from the sinus. In the ordinary case local immunity eventually becomes established and with the recession of edema the drainage passageways open up to permit an outflow of purulent secretions as rapidly as they accumulate and spontaneous cure ensues.

Factors which impede spontaneous healing are those which lower a patient's resistance to disease and local conditions which block sinus drainage. Those usually mentioned as being contributory to the persistence of sinus infection are the weather, the patient's habits, his indulgences, his temperament and psychic make-up, allergy, gastro-intestinal disturbances, nutritional deficiencies, endocrine imbalances, debilitating diseases, infections elsewhere, especially in neighboring sinuses, and various other items which should include also improper medical and surgical therapeutic measures.

Local factors are those which interfere with normal sinus drainage. The defects may be in the ostium itself or at other points along the drainage passageways. The lumen of the maxillary ostium may be filled with a polyp or constricted in varying degrees by acute or chronic inflammatory or allergic edema which may reach the point of complete occlusion.

Further impairment of drainage may be caused by the presence of polyps adjacent to the ostium, either in the sinus itself or in the middle meatus. It may be caused by a swelling of the tissues which

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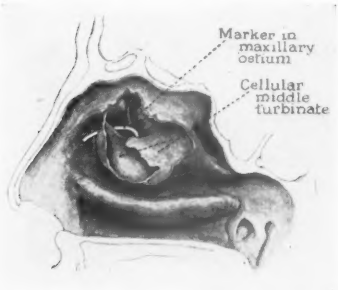

Fig. 1.—Cellular Middle Turbinate. The specimen illustrated shows an extensive pneumatization of the middle turbinate. The area adjacent to the maxillary ostium is completely blocked off.

line the ethmoid infundibulum or by a middle turbinate which commonly is wedged tightly against the lateral nasal wall.

In an inflammatory process of the maxillary sinus, the products of the infection are removed by the mucociliary mechanism of the sinus mucosa. The exudate is carried up the wall, through the ostium to the infundibulum and thence to the nasal cavity. Clumps of exudate occasionally are too heavy and thick to be readily compressed into a narrow drainage space and may drop back to the floor before reaching the ostium. At times thick clumps are wedged for some time in the lumen of the ostium, causing pain over the sinus. This, according to the experiments of Hilding,[1] is caused by the development of negative pressure in the sinus, occurring when an occluded ostium prevents air from reaching the cavity.

The same investigator has shown that the cilia which line narrow tubes are capable of exercising a powerful force on plugs of mucus which occlude the lumen of the tube. Masses of exudate caught in the constricted drainage channels of the maxillary sinus in this manner eventually are moved along by the combined action of cilia which face each other across a narrow space. Relief of pain occurs immediately with the dislodgement of the plug.

In cases of retarded drainage, recovery is prevented. Drainage is taking place but too slowly to produce a removal of the secretions as rapidly as they accumulate and many cases are thus prolonged to a subacute or chronic state.

Fig. 2.—Cellular Middle Turbinate. The large cell in the specimen illustrated contains 2 cc. of iodized oil which depicts its extensive growth in all directions. A cell such as this and the one shown in Fig. 1 may be crushed or eliminated by removal of its lateral wall.

The intimate relationship of the ostium to the structures in the middle meatus is evidenced by examination of specimens from cadavers. An occasional specimen discloses the result of an infection of the antrum by the gross appearance of its lining membrane which is thickened and irregular. In these specimens, the mucosa lining the ostium and the infundibulum is also involved in the process.

In any large group of specimens, examples may be found in which there is a complete absence of antral drainage space. In these cases the uncinate process has become adherent to the bulla, obliterating entirely the hiatus semilunaris, and the ostium has been narrowed to a minimum by the thickened membrane which lines it.

Such cases are encountered occasionally in clinical practice. Probing the middle meatus with a cannula reveals the presence of an occluded hiatus with an entirely inaccessible ostium. Irrigation of the sinus by means of puncture through the middle or the inferior meatus is impossible for there is no outlet for a return flow of the solution.

Chronic Maxillary Sinusitis. In the management of maxillary sinusitis of a few months' or several years' duration the rhinologist

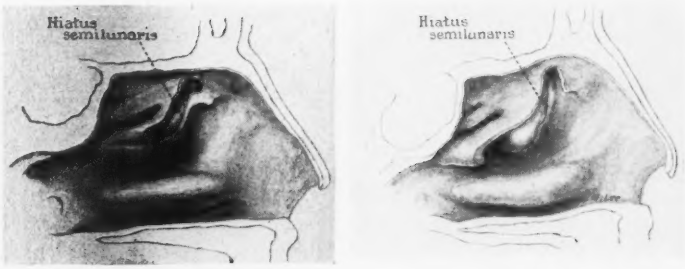

Fig. 3.—The Sealed Hiatus Semilunaris. In each of the specimens illustrated the hiatus semilunaris is completely sealed off by thickened mucosa covering the bulla and the uncinate process. These two structures are normally separated by a distance of 2 or 3 mm.

In Specimen B. the bulla protrudes below and medial to the uncinate process and this anatomic entity contributes somewhat to drainage impairment.

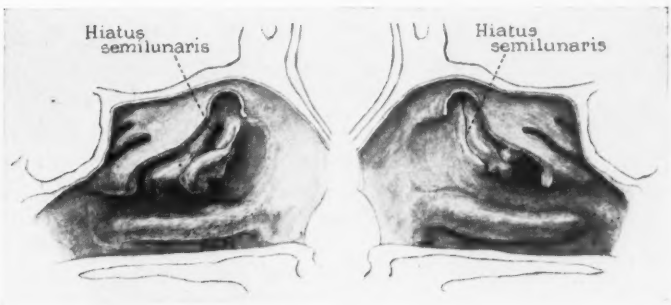

Fig. 4.—Blocking Polyps. Polyp formation obstructing the drainage of both maxillary sinuses. The mucosa of both antra is thickened and the gross appearance is that of a chronic inflammatory process.

must at the outset discard any ideas which he may be harboring concerning the ineffectiveness of conservative measures in chronic sinus disease.

If he is one who commonly advocates the Caldwell-Luc procedure because a few irrigations have failed to effect a cure or feels that a thickened antral mucosa as revealed by x-ray study is in itself sufficient indication for its radical removal, then he should set about to acquaint himself with some of the capabilities of the membranes which line these cavities.

The swelling noted on roentgen examination is the normal tissue reaction to disease and the swelling remains as long as the membranes are subjected to irritants, whether they be pathogens, allergens or merely the toxic irritation of a stagnant exudate such as is always present in poorly draining infected cavities.

It has been fairly well established that these membranes are disease resisting rather than diseased membranes. This may be determined by microscopic examination of sinus mucosa removed at operation. Although thickened and irregular in structure they present every characteristic of tissues which are able to return to normal under favorable conditions.

Conditions conducive to such a restoration are attained only by correction of drainage defects so as to permit a constant unhampered flow of secretions from the sinus cavity into the nose.

Recently the writer reported the results of a study of sections of tissues removed from 82 patients by radical procedures.[2] In the entire group there was no membrane which could be designated as being diseased beyond hope of repair. In no case were there signs of abscess or ulcer formation and in most an intact epithelium was present along with a stroma showing active proliferation with tendency to heal. In a majority of cases, allergy was manifested by the presence of eosinophiles in varying degrees, and this would indicate that allergy is a dominant factor in the maintenance of chronic sinus disease. In others, lymphocytes and plasma cells predominated, indicating simple chronic infection; while in the chronic suppurative types, polymorphonuclear leucocytic infiltration was superimposed on a chronic proliferative process.

In the study of the 82 cases, the subsequent history showed that few of these patients obtained other than temporary improvement from the radical procedures. The records indicate inadequate preoperative care in most cases. Had this been carried out, there is little

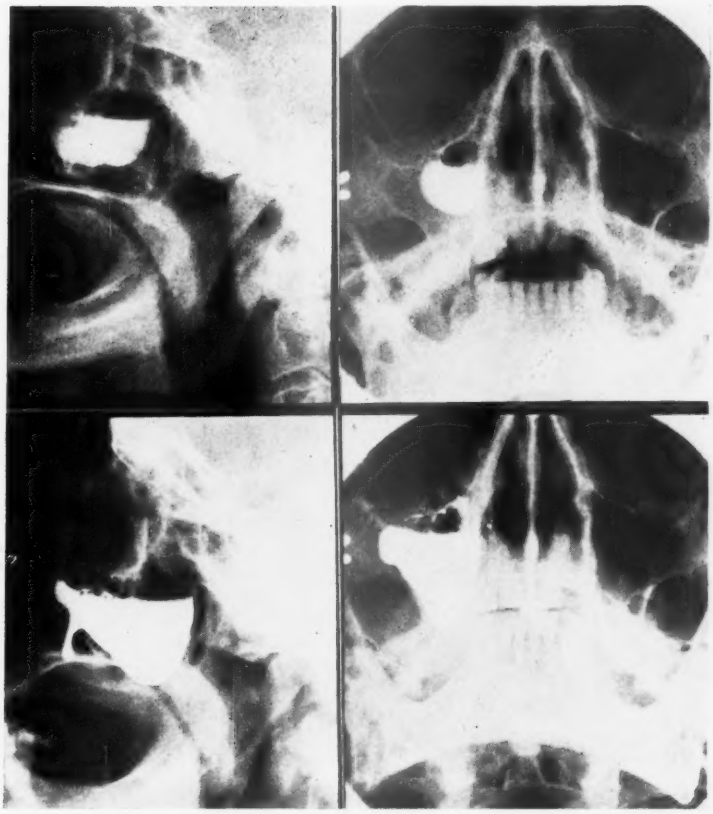

Fig. 5.—Recession of Edema. The films reproduced above show in the upper two films lateral and frontal views of a patient with chronic right maxillary sinusitis. Infraction of the right middle turbinate with weekly irrigations followed by instillations of iodized oil produced a diminution of edema and absence of symptoms in five months.

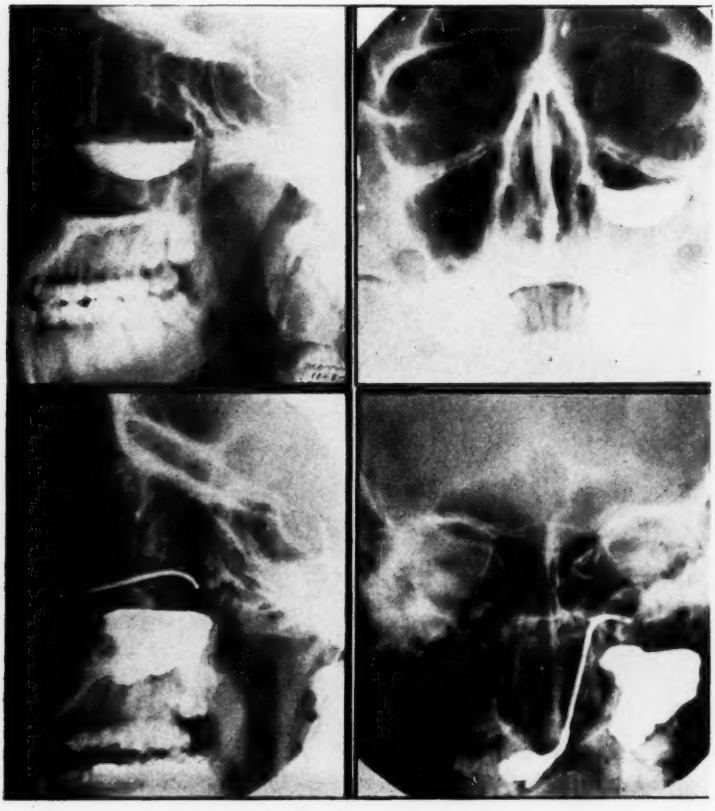

Fig. 6.—Similar result to that in Fig. 5. This case was one of pansinusitis and it was necessary first to clear up the infection in the left frontal sinus before the treatment of the antrum was effective.

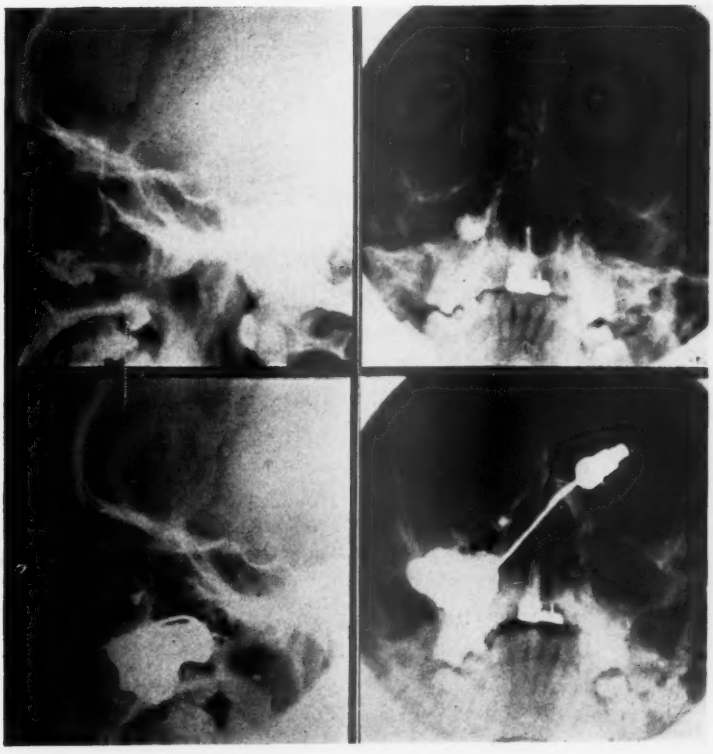

Fig. 7.—Marked thickening of the antral mucosa is shown in the upper two views taken February 7, 1944. Absence of edema may be noted in lower films taken April 10, 1944, two months later. All evidence of chronic sinusitis had disappeared by that time.

question but that many radical procedures would have been avoided and the group as a whole would be in far better shape than they are today.

On the other hand, the results obtained by conservative management have been entirely satisfactory. With the establishment of adequate drainage facilities, all cases tend to clear up; the exudate disappears and the sinus mucosa regains its normal appearance. This improvement may be noted by sinus lavage and roentgen studies with iodized oil in the cavity and subjectively by a diminution of symptoms.

In the proper management of maxillary sinus disease, regardless of the type or stage, the simplest measures to effect a cure are instituted.

In a surprising number of cases the measures required are indeed simple. Many respond favorably to no other treatment than infraction of a middle turbinate or the removal of a few polyps. In some cases the first step is correction of a deviated septum so that the middle meatus may be unblocked. All patients should, however, receive an allergy study at the outset and it has been determined that stubborn cases are more than likely those in which allergy control has not been attained.

Persistent infections may often be traced to an overlooked infection of ethmoidal, frontal or dental origin or progress is retarded by some systemic disorder which has been overlooked or neglected.

In those cases which fail to show improvement despite the correction of all drainage defects, intranasal antrostomy is advocated. An improvement in the symptoms usually follows immediately and in most cases a complete cure results. If the infection persists it is because the window is inadequate, because a coexisting infection in some other locality is draining into the antrum or because of an uncontrolled allergy or some other systemic condition.

SUMMARY

The maxillary ostium in a healthy state provides an adequate drainage outlet for the maxillary sinus.

During an inflammatory process involving the sinus, mucosal swelling constricts the lumen of the ostium to retard or block completely the discharge of pus from the cavity.

Recovery takes place as the edema recedes sufficiently to permit an outflow of secretions as rapidly as they accumulate.

A prolongation of infection is caused by factors, local or otherwise, which cause drainage impairment.

Defects may occur in any portion of the drainage passageways from the ostium to the nasal cavity, but commonly are those which cause a blockage of the middle meatus. This may be induced by an impinging middle turbinate, obstructing polyps, or as is often the case, by the generalized mucosal edema of an uncontrolled allergy.

In the management of chronic sinus disease, then, the role of the rhinologist is fairly clear. He is to adopt measures for the correction of drainage defects sufficient to permit an unhampered flow of secretions from the sinus.

In cases which fail to respond after all apparent barriers have been removed, an intranasal antrostomy is indicated.

This procedure properly carried out is effective in a large majority of cases and failure implies an inadequate window, an overlooked infection focus of dental, ethmoid sinus or frontal sinus origin or some overlooked or uncontrolled systemic condition.

The radical removal of sinus mucosa offers little more than temporary relief and is not indicated in the long range management of chronic maxillary sinusitis.

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LXIX

GENERAL FACTORS IN IRRADIATION THERAPY

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For all practical purposes a general review of the facts known about x-ray and radium is all that is profitable in this brief review. While it is true that there are other and perhaps very valuable methods of irradiation, most of these have no general use at present and are still under investigation. To this category belong neutrons and the radioactive substances produced by neutron bombardment.

The essential difference between irradiation and other physical and chemical instruments rests on two properties; first, the rays penetrate solid substances such as living tissues and can be concentrated at any depth in the living body, and second, cells and tissues differ widely in their tolerance to irradiation. Irradiation may be so weak that no demonstrable changes in cells or tissues can be observed. It may be so strong that all cells and tissues which it strikes are completely destroyed. Therapeutic irradiation lies between these two extremes. Where two or more tissues exist side by side or are actually intermingled and one is pathological and the others normal, it may be possible to destroy entirely the pathological tissues without serious injury to the normal tissues. It is probable that all cells and tissues are injured by irradiation. However, if the amount of irradiation is not lethal, the tissue or cell has the power of recuperating and returning to normal.

X-rays and gamma rays of radium, rays of ordinary visible light, ultra-violet rays and infra-red rays, as well as radio waves, all belong to the same order of things. They all have the same speed, 186,000 miles per second. They have no electrical charge. They can be polarized, reflected and diffracted. All of these phenomena can be explained by the wave theory of light. However, there are other observed characteristics that are much better understood by the assumption that all of these waves are made up of extremely small particles of matter traveling at enormous speed. As a matter

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of fact, the two theories have to be combined for an adequate explanation of all the observed effects. The particular theory is not new but in its modern form is known as the quanta theory.

The only difference between these different waves is their frequency or wave length. The shortest wave lengths are obtained from the gamma rays of radium and from extremely high voltage x-ray. There is a direct relationship between the wave lengths and the energies of the quanta. The shorter the wave length, the greater the energy. .

The unit of measurement for wave lengths is one ten-thousandth of a centimeter and it is called the Angstroem unit. Gamma rays from radium vary from 0.02 to 0.1A, roentgen rays vary from 0.01 to 5.00A.

From radium preparations, in addition to gamma rays, there are two other kinds of rays known as alpha and beta rays or particles. A large part of the energy emitted in the form of irradiation by radium is in alpha rays. These rays have so small a penetrating power that they are completely absorbed in the first few centimeters of air or by a thin sheet of paper. Owing to this failure of penetration alpha rays have only a very limited use in therapy. The alpha rays from various ray-emitting substances have different speeds, varying from 9,000 to 20,000 miles per second. From any one substance, however, all have the same speed. Alpha rays have been identified as helium nuclei.

Beta rays vary greatly as to speed. Some closely approach that of light. They carry a negative charge. They have considerable power to penetrate matter. A small fraction of an incident beta ray irradiation is present after passing through 2 cm. of tissue. Approximately seven per cent of the initial beam is present after penetrating one cm. of tissue. All beta rays are absorbed by .5 mm. of platinum or 2 mm. of brass or monel metal. As will be discussed later, beta rays are very valuable in treating many superficial conditions amenable to ray therapy.

From the crude apparatus which Roentgen used to discover x-rays in 1895 there has been an almost unbelievable development of x-ray apparatus and tubes. As fascinating as an account of this development would be, it must be omitted here. The x-ray machine takes the ordinary street current, reduces the amperage and raises the voltage to any desired level. It removes the reverse current and is passed through a highly vacuumized tube as a direct pulsating

current. In the tube is an anode, usually called a target, and a filament called the cathode. The cathode is heated and when a current is passed, rapidly moving ions fly from the cathode against the target. The impact of these particles produces x-rays. Only about two per cent of the energy of the employed electric current is transformed into x-rays. This is the reason that cooling of x-ray tubes is necessary. Most of the energy is dissipated in heat.

The shortest wave length emitted by an x-ray tube is directly proportional to the voltage used in producing the x-rays. In ordinary deep therapy from 250 K.V. to 400 K.V. is now employed. For very superficial therapy peak voltages as low as 10 K.V. are used. For a number of years 1,000 K.V. apparatuses and tubes have been in use. At present 2,000 K.V. outfits are available and indeed arrangements for using voltages all the way up to 100,000 K.V. can be constructed. Little, however, is known as to the therapeutic value of these very high voltage apparatuses.

By far the most accurate method of measuring the quantity of x-rays is by the ionization method. At the present time it is possible to secure measuring instruments which are easily used and extremely accurate. The unit of x-ray quantity which has been universally adopted is represented by the small letter "r" and is called a roentgen. Ordinary air when subjected to irradiation becomes ionized and due to the fact that free ions are liberated from the atoms composing air, the air becomes electrically conductive and the strength of the current is directly proportional to the amount of ionization. Under fixed conditions of temperature and pressure an r is the amount of ionization which is produced in one cubic centimeter of air. With the remarkable stableness of our apparatuses of today as to output of x-rays and the methods employed in measuring x-rays, there is little or no excuse for x-ray burns and injuries.

The quality of the x-rays is usually expressed in stating the thickness of a metal filter which reduces the quantity of irradiation to one half. This is ordinarily called the half value in copper, aluminum, etc.

Filter is the term applied to any material placed between the x-ray tube and the object being irradiated. Primary filters are usually metals, while secondary filters are organic substances.

When an x-ray tube is in operation the rays are emitted in a continuous spectrum. The shortest wave length is directly proportional to the peak voltage. Extending downward from this

shortest wave length, every wave length to those corresponding to very low voltages can be observed. The quantity in different sections of the spectrum is about the same, except in the region of the characteristic radiations. Here there is a great increase in the intensity of the radiation. This K radiation, so far as position in the spectral band is concerned, varies with the metal employed in the target of the x-ray tube. In the case of tungsten, the K radiation corresponds to a voltage of 80 K.V.

What a metal filter does is to remove the longer wave lengths completely and to reduce all the wave lengths. It is obvious that this reduces the quantity of rays but increases the penetration due to the fact that the average wave lenth is shorter. In ordinary deep therapy a filter thick enough to remove all K radiation and everything below this level is employed. This first metal filter is called the primary filter. However, a secondary filter should also be used and this should be of some light organic material, such as rubber or bakelite. The reason for this secondary filtration is that ions are liberated from the filter when x-ray is passed through it. These particles have but little power of penetration but can produce irritation of the skin if a human being is being irradiated. The quantity, as well as the energy, of these secondary ions is directly proportional to the density of the filter.

As the density of metals increases so does the capacity of absorption. Roughly the absorption is proportional to the cube of the densities.

We have already commented on the very low power penetration of alpha rays. If a preparation of radium or radon is surrounded by a filter of 2 mm. of copper or brass or the equivalent thickness of any other metal, all the beta rays are absorbed by the filter. When high penetration is desired it is very important to remove by filtration all beta rays and some of the softer gamma rays. Gamma rays from radium have a capacity of penetrating great thicknesses of very dense metals; for example, there are still present a small percentage of these rays after passing through twelve inches of lead. Beginning with a filter which removes all beta rays the filter may be made thinner and thinner and with each reduction in thickness the quantity of beta rays is increased. More will be said about this in succeeding paragraphs.

Peak voltage has already been defined. Effectual voltage represents an average voltage or the voltage which would give the same penetration if a continuous homogeneous voltage is applied to a tube.

The effectual voltage is usually estimated at about one-half of the peak voltage. The effectual voltage corresponding to the wave lengths of radium is approximately 1,000 K.V.

Radium rays are emitted spontaneously from certain elements. Practically all elements with an atomic weight of 208 or more possess this property. There are three groups or families of such elements. Radium belongs in the uranium family. The other two groups are thorium and its decomposition products and actinium. There are at least 40 or more of these elements known.

The parent of radium is uranium. Uranium in small quantities is present in the crust of the entire world and in sea water. In much larger quantities it is found in a number of minerals.

Radium can be separated from uranium by chemical and physical procedures. It is usually sold as a salt of one of the well known acids. Radium chloride, bromide and carbonate are soluble in water. The sulphate is insoluble.

Starting with uranium, whose atomic weight is 238, and ending with lead, whose atomic weight is 206, there is a continuous series of transformation.

A radioactive element is in equilibrium with its products when the amount of each product is always the same. Radium, for instance, is in equilibrium with uranium when there is one gram of radium to 2,830,000,000 grams of uranium. There are two kinds of transformations; first, those in which a helium nucleus is removed from the atom. When this occurs an alpha ray is liberated and the atomic weight reduced by four. The other change is one in which only beta and gamma rays are emitted. These are always together. The atomic weight is not changed but a new substance is formed which is termed an isotope. Between uranium and radium there are six of one or the other of these transformations and between radium and lead there are ten such changes. The atomic weight of radium is 226. Consequently in going from uranium to radium there are three alpha ray transformations.

The disintegration of a radioactive element is perfectly uniform. The same number of atoms are affected in a unit of time. What determines why this should be is not clear. None of the ordinary laboratory methods have any capacity to change the rate of disintegration. It occurs in liquid nitrogen or at very high temperatures without any change whatever. Bombardment with neutrons would undoubtedly produce alterations in this rate of disintegration.

The more rapid the disintegration of an element, the greater the amount of radiation. The rate of disintegration is usually expressed by stating in time the half value period. For example, the half value period for uranium 2 is 2,000,000 years, for radium 1,690 years, for radon 3.85 days and for radium A, B and C it is a matter of minutes.

Freshly prepared radium gives off only alpha rays and when it is placed in a glass or metal container all these rays are absorbed by the container itself. The same is true of radon. All of the useful rays from a radium preparation come from radium A, B and C.

When freshly prepared radium is sealed in an air-tight container, it reaches equilibrium with its products in 30 days and unless lost by breakage or other accident remains essentially constant for long periods of time.

It is obvious from what has been said that the rays from radium and radon are identical. Radon may be separated from radium in a number of ways. We have found that a highly efficient and convenient method is to put radium chloride into solution in slightly acidulated distilled water. This solution is placed in a flask which is joined to a vacuum pump or pumps. Every day there is produced a definite quantity of radon, helium, oxygen, hydrogen and water vapor. By means of the pump or pumps these gases are removed from the flask. First, the water vapor is taken up by potassium hydroxide. Then the hydrogen and oxygen are combined by sparking in a special chamber. In this way several hundred cubic centimeters of gas are reduced to four or five cubic centimeters. This residual gas is passed into an inverted tube and transferred to another apparatus which has been completely evacuated. The gas is drawn into the vacuum and by means of a mercury column brought into a special spiral tube which is surrounded by liquid nitrogen. By this means the radon is frozen to the walls of the tube. The other gases can be removed since they are not frozen. Finally by removing the liquid nitrogen the radon is thawed out and transformed from a solid back into a gas. This small quantity of radon is then pushed into any desired container and sealed off. Usually in our work it is placed in a glass bulb with an internal diameter of 3 mm. Into such a bulb at least two hundred times as much radon can be placed as the radon which is found in equilibrium with a radium salt. We have frequently made bulbs containing 2,000 mc. of radon.

Both radium and radon apparatuses have advantages and disadvantages. The advantage of a radium apparatus is that the out-

put of radiation is constant as long as the apparatus is intact. When a treatment is completed all that need be done is to place the radium apparatus back in the place where it is stored until the next time it is used. The disadvantages of radium apparatuses are that there is always the danger of loss by breakage, by sterilization and that insurance rates are relatively high.

The advantages of radon are that there is very little danger of loss, that there is great plasticity as to the strength, shape and size of apparatuses. It is ideal for all kinds of experimental work. Sterilization is more adequate and much less hazardous and the insurance rates are low.

The disadvantages of radon are that it demands operating a radon plant, developing technicians and making daily measurements as to quantity and tables showing the changes in an apparatus from day to day or from hour to hour.

Where work is in a limited field, such as for example treating adenoids in the nasopharynx, a radium applicator would seem to be much simpler and more convenient unless a very large number of patients have to be treated each day. On the other hand, in an institution where all kinds and conditions of problems are met, a radon plant is more convenient.

In the measurement of radium rays, the measurement of an unknown quantiy of radium is made by comparing its ionization to that of a known quantity. This can be done in a number of ways but the simplest method is with an ordinary gamma ray electroscope. The first standard was made by Madam Curie in Paris. A perfectly pure radium salt was obtained, accurately measured as to quantity and its gamma ray output determined. From this standard, subsidiary standards were made for a number of governments. Our standard in this country is at the Bureau of Standards in Washington. It is highly desirable for those operating radon plants and using radon apparatuses to have a standard made to correspond with the standard at Washington.

The amount of gamma rays emitted by one milligram of radium and one gram of radium are as one to a thousand. Radon is compared with radium by determining its gamma ray output. When the output is exactly the same as that of one milligram of radium it is called a millicurie and when exactly that of a gram of radium a curie. As already stated, the quality of radiation from radon and

radium are identical. Both are the rays given off by radium B and C.

Regarding the recording of radium or radon dosage, we have already stated that x-ray is measured in r units. Measuring gamma rays in r units has proven quite difficult. However, one milligram of radium at a distance of one centimeter gives approximately 7.75 r per hour. It is not practical, however, to use the gamma rays on the r basis. What has to be annotated is the amount of radium, the filtration, the distance from the surface and the duration in time of the exposure. Where it is desired to give the dosage in a volume in the depth of the body, in addition to the data already stated, the actual size of the volume and its shape, its distance from the surface and the distribution of the sources of radiation must all be stated.

What happens to rays which penetrate a solid such as the human body? Some of the rays pass straight through unchanged. Certainly these have no biological effect. The same may be said of the scattered rays which emerge from the body in various directions unchanged. Thinking of the rays as quanta some may be completely absorbed. Others lose only a part of their energy and proceed as waves or quanta of longer wave length and less energy. It is practically certain that the rays which are absorbed, either in whole or in part, produce ions and that these ions cause the biological changes in tissues. These particular ions are called photo-ions and their energy depends on the energy of the x-ray of gamma ray quanta. A single photon can dislocate ions from a number of atoms.

There is no direct way of measuring ionization in the living body. What takes place can be approximated by taking measurements in phantoms of the same specific gravity as human tissue. Water and various other substances have been used for this purpose. Careful measurements can be thus made at various distances from the surface of the body and the measurements correlated and annotated in isodose curves. Exactly similar curves may be made for radium in considerable quantity used at from five to fifteen centimeters from the surface of the body. This particular type of radium radiation is known as tele-radium. It apparently has little or no superiority to x-ray and has been almost entirely replaced by x-ray treatments.

The chemical and biological changes which follow the absorption of roentgen and radium rays are as follows. Both clinical and experimental observations indicate that irradiation is always an injurious agent and never a direct stimulant. It is true that radiation

which is not lethal and where recovery is rapid may be followed by overactivity in growth and other functions. This is not peculiar to irradiation but often follows other types of injury. Two factors, first, the intensity of irradiation and, second, the capacity of the body to repair injuries incident to irradiation, determine in large measure what is to be expected from a given exposure to the rays. If the radiation is short of being a lethal amount, one can expect ultimately a return to normal and the effects are quite different as the time of exposure varies. A given amount of irradiation given in a few minutes may produce a violent reaction on the skin, whereas if the same amount be given in a period of three weeks no reaction may occur. It is certain that many malignant tumors which happen to be less tolerant to radiation than the normal tissues which surround them can be much better treated by some method of prolonged irradiation than by a single short massive dose. It seems that the tumor in such cases has less power of repair than the normal tissue. This rule, however, does not hold for all clinical effects and also cannot be relied on in all laboratory experiments. This is evidenced in experiments both on fruit fly and Ascaris eggs.

The changes both gross and microscopic which take place in cells and tissues after irradiation are not specific and are observed following various other injuries. Following irradiation the first morphological changes are observed in the nucleus of the cells. Mitosis and cell division are brought to a halt. The protoplasm of a cell body soon becomes granular. With the ideal irradiation there is not destruction of the cell or perhaps even shortening of the cell life, but prevention of reproduction. It is possible that this is the effect observed in treating the nasopharynx with the nasal applicator to remove adenoid tissue and secure better ventilation of the middle ear. Some of the early laboratory work suggested that cells were more sensitive at the time of mitosis than at other times and also that in the case of tissues the sensitivity was inversely proportional to the degree of differentiation. Up to the present time these facts have not been of help in clinical treatment. Many tissues which are actively growing and show marked mitosis are very insensitive to irradiation and exactly the reverse is found in other tissues.

Certainly there are great variations in radiosensitivity between different cells and tissues and indeed individual cells of the same type may vary greatly. A very moderate irradiation may destroy a half or more of the cells of a given tissue, but to destroy every cell may require four or five times the amount of radiation. At the present time there is no adequate explanation for these variations in sen-

sitivity. They are observed in all experimental material, such as fruit fly eggs for example.

The latent period is a term applied to the period of time which elapses after irradiation before definite morphological changes can be observed. The length of the latent period varies inversely with the intensity of the irradiation. If we take the human skin as an example, a slight erythema may occur as late as three weeks after a mild radiation, whereas with a very intense radiation it may develop in a few hours. In highly sensitive cells and tissues definite morphological changes may be found by microscopical examination after a few hours, even when the radiation has been very mild. These first changes involve both the nucleus and the cell body. Physiological changes are more difficult to observe and evaluate. However, definite changes in metabolism, increased permeability of cell membranes leading to edema and increased acidity are all common occurrences.

Reasoning on the analogy of the effects of ordinary light, television, and other forms of light, it was believed that very different effects might be observed depending on the wave lengths employed. The preponderant weight of opinion today is that there is no qualitative difference in effect between wave lengths, and that both the morphological and physiological changes will be the same if the same amount of radiation is absorbed. This of course does not mean that the character of the radiation inside the body as produced by different qualities of radiation is the same. However, there seems to be very little, if any, advantage gained in clinical results by increasing the voltage from 300 to 400 K.V. to 1,000,000 K.V.

For the protection of personnel in treating patients, it is easily possible where x-ray is used to cut off all radiation from the persons who operate the x-ray machines with suitable thicknesses of lead. This should always be arranged for. The construction details and the protection necessary can readily be found in any modern work dealing with x-ray therapy. Before considering protection from radium or radon preparations it is well to recall that the time of exposure, the strength of the applicator, the distance of the applicator from the operator are all facts which it is essential to know. To these factors must be added the protection afforded by lead screens and covers.

The best way of protecting the hands and fingers against beta rays is afforded by cutting the time of exposure to a minimum and using forceps to secure as much distance as possible. The radium applicator should be kept in a hollow lead cylinder whose wall thick-

ness should be from one and a half to three inches across. This cylinder should be mounted on a movable hand truck. The truck can be rolled up to the treatment table.

Gamma rays are more likely to cause internal injuries. The earliest changes observed are in the blood count and in the effects on the generative organs. In addition to the precautions already listed, the length of service of nurses and technicians who make up the applicators should be limited as to time.

It may be of interest to calculate the actual exposure in roentgens. A thousand milligrams at one centimeter in one hour give 7,750 r. Like all other forms of light the intensity varies inversely with the square of the distance from the source of radiation. For example, if a gram of radiation material is 100 cm. from the point of measurement then the radiation produced by the one gram in one hour would be only .78 r, at 200 cm. only .19 r. per hour. It is obvious from these calculations that even when dealing with large quantities of radium that over-radiation is almost out of the question provided the protective measures outlined be followed. Five cm. of lead reduces the radiation to 7.5 per cent which means that if two applicators are used, each containing 50 mg., the actual radiation is the same as that of 7.5 mg. when no lead is used. Behind the two inch lead screen at two feet only .1 r is given.

Just how much irradiation the human body will tolerate is an open question, but taking .03 r per hour, which is about as much as any one operator would get in a single day, and using it every day for a year the dosage would only be about 90 r.

At the clinic where I am associated there has never been a serious general injury. In the early days moderate reduction in the white blood count did occur, but when the individual was moved from the work it promptly returned to normal. There have been no cases of sterility, no cases of genetic change in children.

It might be of interest to know that we have been using from five to six grams of radium for approximately 30 years and in the first ten years had nothing like the protection we have today.

In this paper we are not considering details of treatment and clinical results obtained but are outlining some of the guiding principles which should be followed in employing irradiation as a therapeutic procedure.

While the results are the same if an equal absorption is obtained with radium or x-ray, in actual clinical practice the application may

be much simpler with one or the other, or even impossible with one and readily accomplished with the other. We have already covered the essential reason for these differences. Spherical dispersion which accounts for the inverse square law is the basis of many of these differences in usage. The aim of treatment always is to cure and not injure the patient. In ophthalmology it is particularly vital not to injure any of the essential structures of the eye upon which vision depends. In nose and throat work injury of bone, cartilage and nerve tissues must be considered and the radiation planned so as to reduce to a minimum the possibilities of such injuries. In otolaryngology, as well as ophthalmology, the beta radium applicators are particularly valuable in treating superficial lesions. Where deep-seated and extensive lesions are concerned, such as may occur deep in the orbit, in the sinuses, in the tonsils, in the larynx, in the pharynx and nasopharynx, x-ray is the best agent. By careful location of the pathological lesion, its depth from the surface, its shape and size, it is possible by using multiple portals of entry through the skin and cross-firing to give quite intensive dosage where this is needed. I would like to point out here that in the treatment of malignant neoplasms x-ray should be considered as a surgical instrument, this is particularly true of the more ray-resistant tumors. There are only a few of these growths that can be eradicated by a general spraying of the entire field. These are of course the supersensitive tumors such as lymphosarcoma and lymphoblastoma. This viewing of the necessity of using portals just large enough to take in the entire lesion being treated cannot be emphasized enough. Actually to carry out exact cross-firing with small portals demands time and patience. It cannot be turned over to a technician as is so often the case. One frequently sees portals 10 cm. in diameter employed in treating a growth which is less than 1 cm. in diameter. This inevitably means over-radiation of normal tissues and injuries which may not show up for years.

Inflammatory conditions when treated by x-ray never require heavy dosage. In general the benign tumors can be better treated by some surgical procedure. Most of them are quite ray resistant. Benign lymphomas and angiomas are an exception to this rule.

Radium by direct application or implantation in suitable locations is much more desirable than x-ray. The inverse square law makes it possible to give direct radiation of any intensity decided on to the pathological tissues, and at the same time to give very little radiation to surrounding normal elements. Implants are very small tubelets of radon which can be left in permanently or easily removed

as seems best. The filter, usually .3 mm. of platinum, removes the beta rays almost entirely. Where there is an accessible solid mass, the ideal method of treatment is to divide it into spheres and attempt to implant in each sphere a radon point strong enough to give adequate treatment to tissues on the surface of such a sphere. Implants can readily be used in the treatment of lip, tongue, floor of the mouth, cheek and tonsil conditions, as well as in the glands of the neck which have been secondarily involved. In general, implants should only be used for treating malignant growths. Radon or radium can be used in conjunction with a surgical approach for treating malignant conditions of the head sinuses and of the orbit after removal of the eye.

X-ray and radium can often to great advantage be combined to secure adequate radiation therapy. It should also be constantly kept in mind that certain conditions which may not be suitable for operative treatment become so after the effects of radiation have fully developed. While not a cure-all for any type of lesion, irradiation can bring relief to many conditions and often cure where no other agent can accomplish such a result. The advantages and disadvantages of radiation as compared to surgery where both may be effectual must be carefully weighed and determined as to the more suitable by experience. Certainly in the malignant tumor class all of these cases which obviously cannot be cured by surgery should be given the advantage of ray treatment, since some of them will be cured.

Nasal applicator and the beta ray applicator. Dr. Crowe and I originally used a nasal applicator with a wall thickness of 1 mm. Our feeling was that a better distribution of the radiation in the nasopharynx could be secured by such an applicator which emitted only gamma and a few very hard beta rays. The disadvantage of this applicator was that it required for short treatments a great deal of radon and the treatment could not be accomplished at all where radium was used except by long exposures. By reducing the wall thickness from 1 mm. of brass to .3 mm. the time of the application has been reduced to about one sixth of that required when 1 mm. of brass is used. Monel metal which has the same absorption power as brass but has other qualities that are better than brass was selected as the screen. This made it possible to make a radium-containing applicator and yet not unduly prolong the time of treatment. In addition to this, there is the economic factor. Radium is an expensive material and it means a good deal to cut the essential amount needed to one sixth of what would be required with the thicker screens.

Whereas approximately a gram twenty-three seconds is required for a unit dosage with the nasal applicator, with the so-called beta ray applicator devised for superficial work in ophthalmology an approximately similar dosage can be secured in a gram two seconds, if there is no screening except the glass containing the radon. It is possible, however, to use screens of various thicknesses of aluminum if it is desired to remove the softer beta rays. The best method of determining the safe method of dosage where any change is made in the applicator, is to determine the time necessary to produce a mild erythema on the skin. Physical methods of measurement are not very satisfactory.

Remarks on Annotations: We have already remarked on how radium and x-ray treatments should be recorded. Usually radium applications are recorded as so many milligram hours, milligram minutes and milligram seconds. We have found it more convenient to express the dosage in gram hours, minutes and seconds. For instance where gram seconds are considered the amount of radium or radon used is divided into 1,000. Let us say the amount of radium is 50 mg. Then the quotient will be 20, and 20 seconds exposure with the applicator used will give 1 gram second. This 1 gram second can be again multiplied to give any desired number of seconds.

CONCLUSIONS

I trust I have made it clear that irradiation can be used to advantage in a great many clinical conditions both in otolaryngology and ophthalmology, that it is simply a method of treatment, just as is a surgical procedure or the use of bactericidal and bacteriostatic drugs. The specialists in ophthalmology and otolaryngology should master the principles of ray therapy and either carry out the treatments themselves or have them carried out in the way that is likely to produce the best results. Initially, practically all patients suffering from new growths, benign and malignant, and from various infections come to the specialist. He is in a position to study and assess the value of therapeutic procedures, and as experience is accumulated to change and adjust methods to secure better and new results. So far as the beta ray applicators are concerned their use is so simple that any competent man can take them up with very short study and instruction and apply them clinically. With x-ray and with implanting, cooperation between a competent radiologist and a specialist is perhaps the best method of procedure.

Finally for those who decide to take up this form of therapy, it is urged that all the suggestions made as to protection of patients

and of personnel be most carefully and scrupulously carried out. If this is done there should be no method of treatment safer or simpler in its employment.

THE JOHNS HOPKINS HOSPITAL.

LXX

IRRADIATION OF THE NASOPHARYNX

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Until recently textbooks on otolaryngology devoted very little space to the underlying causes and the prevention of upper air passage infection, but were chiefly concerned with the treatment of infection. Particularly was this true in the case of recurring attacks of otitis media, sinusitis and allergic bronchitis in children. However, our increasing success in reducing the frequency and severity of upper respiratory infections and preventing chronic sinusitis and changes in the bronchial mucosa that are irreversible and lead to chronic asthma has placed the emphasis upon removal of the cause rather than treatment of the result. The ever increasing routine examination of school children proves more than any other hopeful sign that at last we recognize a great opportunity for preventing conditions which may lead to later trouble. One result of years of intensive study is the conviction that many of the hearing disorders of adult life begin in childhood, and if we are to learn more about the causes, treatment and prevention of deafness we must concentrate our studies on children. Almost every type of middle and inner ear deafness seen in adults is found in children, with this important difference: in children the impairment is just beginning and opportunities are offered for study of the life history of the disease and for developing some kind of effective and even preventive therapy. In adults the malady has been in the making for many years, and the hearing apparatus usually is irreparably damaged. There is much less chance of curing deafness in the adult, and so we must seek in children for a clear understanding of the causes and the best methods of prevention.

This principle of search for underlying causes led to the founding, in 1924, of the Otological Research Laboratory of the Johns Hopkins University, with the aid of the Rockefeller Foundation and

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interested friends. For 20 years we have used in this laboratory the method that has been employed so successfully in studying diseases of the heart, lungs, kidneys and other parts of the body, that is, correlation of history, clinical examination and functional tests with the histologic appearance of the organ after death. By making for research purposes accurate audiometric and tuning fork tests and other examinations of the ears and the upper air passages on patients in the neurosurgical, medical and tuberculous wards whose general condition made it likely they would come to autopsy, we have been able to collect and section serially more than 2000 temporal bones. In a good proportion of these the hearing and the histologic findings were normal, which made them very useful as controls.

The first publication of this correlation study was made after ten years spent in collecting material and preparing sections. The group selected for study had impaired hearing for high tones but good hearing for low tones and for most of the frequencies in the speech range. At that time this type of hearing impairment was universally thought to be due to an inner ear or nerve lesion, and in the majority of our cases this was found to be true. In a few, however, the nerve and the organ of Corti were normal histologically and the only changes seen were in the middle ear. This finding made it very clear that impaired hearing for high tones is not always due to a nerve lesion and led us to reexamine patients, particularly children, thought to have an early stage of nerve deafness. When examined from this new point of view, we began to evaluate the history, the changes found in tympanic membrane, middle ear mucosa, nasal passages and nasopharynx. Many of these children had opacity and retraction of the tympanic membrane, hyperemia of the middle ear mucosa, and a dark purple or bluish discoloration of the drum membrane, which could only be due to a small hemorrhage in the mucosa or to red blood cells and serum lying free in the middle ear cavity. Previously, we had thought these findings, in the absence of pain or symptoms of infection, could not cause deafness in which high tones were more impaired than low tones. It soon became evident, however, that we were dealing with the condition we now call aerotitis, and that the changes we saw could be due only to partial or intermittent eustachian tube obstruction. It was also evident that we must find some method of seeing the nasopharynx and the orifice of the eustachian tubes more clearly than was possible with the laryngeal mirror. Here I wish to acknowledge my gratitude to Dr. Edgar M. Holmes for devising the nasopharyn-

goscope, an instrument which to me just at this time seemed like an answer to prayer. Examinations with this instrument showed an overgrowth of lymphoid tissue in and around the pharyngeal orifice of the eustachian tubes in many of these children and convinced us that some measure other than surgery was necessary in order to remove this tissue without further damaging the tubes.

It had been known for 30 years or more that lymphocytes are extremely sensitive to irradiation, so we turned to Dr. Curtis F. Burnam for advice. He suggested treatment with a radon applicator, constructed the instrument, advised us about placing the applicator and the length of time it could be left in the nasopharynx with safety. Under this treatment the lymphoid tissue around the tubal orifices gradually disappeared, marked improvement or complete return of hearing followed, and in many the bluish discoloration of the tympanic membrane also disappeared. No drugs, inflations or other forms of local treatment were used. The marked improvement in these cases showed conclusively that certain types of middle ear deafness could be cured by this simple, safe, painless and inexpensive method, and also that middle and inner ear deafness cannot always be differentiated with audiometer and tuning fork tests alone.

This was the first of a long series of clinical observations and treatments that has led us to the conclusion that oft-repeated attacks of eustachian tube obstruction are a common cause of impaired hearing in children. Recurrence of adenoids after operative removal is so frequent that it must be regarded as normal. Repeated examinations for research purposes of 1365 unselected public school children showed that adenoids recur in more than 75 per cent of those whose tonsils and adenoids have been removed before puberty, and that nearly 40 per cent of these had either impaired hearing for high tones alone or for all tones in the speech range. In addition to loss of hearing, the regrowth of lymphoid tissue after operation predisposes to recurrent upper respiratory infections, attacks of suppurative otitis media, sinusitis and bronchial infections. For several years we have supplemented every tonsillectomy with irradiation of the nasopharynx. This does not interfere with healing and is desirable, since it aids in the removal of lymphoid tissue in all parts of the nasopharynx and thus helps to reduce the incidence of colds and their complications. The first treatment is given about two weeks after the operation, and two additional treatments are given at intervals of two weeks. With the 50 mg. monel metal applicator the dosage for all treatments is 8½ minutes on each side.

Recurrence of adenoids is not always due to incomplete operation, but chiefly to the fact that lymphoid tissue is an integral part of the mucous membrane of the posterior and lateral walls of the pharynx and nasopharynx and that in some children it hypertrophies as a result of infection, allergy and other causes we do not understand. In the majority of children, however, it regresses spontaneously soon after puberty, without permanent damage. Our task is to recognize early the children who are in need of treatment to help tide them over the childhood years and thus prevent permanent damage that may interfere with their physical development, education and even their careers.

Operative removal of very large adenoids, followed by a series of radium treatments, is always more satisfactory than irradiation alone, because of the mechanical difficulty of applying adequate irradiation to a large mass in this area with the nasopharyngeal applicator. The radium-containing chamber of the applicator is 2 cm. in length and most of the beta and gamma rays are omitted from its sides and not from the end, which is only 2.3 mm. in diameter. When inserted through the nose, the end of the applicator comes in contact with the large mass of adenoids at the choanae. This prevents its further passage into the nasopharynx and leaves most of the radium-containing chamber in the nose. In this position the majority of the rays go into the posterior part of the septum and turbinates; very few of them reach the adenoids. If patients with large adenoids are treated in this way the results will be disappointing. It is decidedly dangerous to plunge the applicator into the mass of adenoids, to bend the applicator, or to construct it with a hinge so the angle of the radium-containing chamber may be changed. This introduces a hazard that the radium-containing part may some day break away and be swallowed or aspirated. If the adenoids are relatively small, however, and it is possible to introduce the applicator far enough into the nasopharynx to permit sufficient irradiation of the tubal orifices, the fossa of Rosenmüller and the lateral walls, then operation is not necessary.

Most infections of the upper air passages begin in lymphoid tissue. It is for this reason that operative removal of tonsils and adenoids is so beneficial in many cases. Lymphoid tissue however, is not limited in its distribution to the tonsils, the middle of the nasopharynx and base of the tongue, but is also an integral part of the mucous membrane of the lateral and posterior walls of the

pharynx and nasopharynx. In many children lymphoid tissue in these locations hypertrophies after operative removal of tonsils and adenoids and gives rise to the condition known as "granular pharyngitis." Often these compensatory hyperplastic nodules, although small in size, are so located that they interfere with the function of the eustachian tubes and cause acute aerotitis media in military aviation, in "escape hatch training" in the submarine service and in other occupations in which men are subjected to extreme pressure changes. The same mechanical abnormality causes in many children a mild and often symptomless aerotitis, which if oft-repeated leads to hyperemia, edema and eventually to scar tissue in the mucous membrane of the middle ear. This impairs the hearing and in the presence of an acute nasopharyngitis causes repeated attacks of suppurative otitis media. We wish to make it clear that we do not advocate indiscriminate use of radium as a treatment for deafness. The hearing may or may not improve, depending on the cause and duration of the impairment. Radiation is of great value in reestablishing the lumen and function of a eustachian tube partially occluded with hyperplastic lymphoid tissue. In other words it is used to correct a condition that predisposes to impaired hearing and to attacks of otitis media. The relationship between chronic or oft-repeated episodes of partial eustachian tube obstruction and impaired hearing is so definite, that irradiation of the pharyngeal orifice of the tubes is justifiable as a prophylactic measure in all patients in whom hyperplastic lymphoid tissue is seen in or near the orifice of the tube. Even if the hearing is normal, irradiation is indicated as a preventive measure when nasopharyngoscopic examination reveals the above conditions. It is also called for in all patients with this condition who have impaired hearing due to any cause whatever, such as developmental abnormality of the cochlea or auditory nerve, chronic suppuration of the middle ear, or otosclerosis, in order to prevent superimposed or additional impairment from an entirely different cause.

Nodules of hyperplastic and infected lymphoid tissue in the nose, near the posterior end of the middle turbinate, may cause symptoms resembling vasomotor rhinitis. We believe lymphoid tissue in this location is a common cause of ethmoiditis and sphenoiditis in children. The acute attacks usually subside with local treatment, but unless the underlying cause is recognized and eliminated the symptoms recur again and again, and result in chronic sinus infection. Lymphoid nodules in the nose and in and around the tubal orifices are often so small that they can be seen only with a naso-

pharyngoscope. They should always be looked for, and if present, removed with irradiation rather than by operation or cauterization. Irradiation is the ideal treatment for chronically infected or hyperplastic lymphoid tissue in locations inaccessible for operative removal. Edema is a constant change following radiation. Therefore, it is advisable to omit treatment when the patient has an acute upper respiratory infection, and in subacute or chronic infections always to give the treatments at three or four week intervals. Otherwise irradiation may precipitate a complicating otitis media or sinusitis. The radium applicator should not be used in the nose itself for any condition except nodules of lymphoid tissue. Polyps are extremely resistant, and the applicator is not suitable for the treatment of malignant growths. It was designed for one purpose alone—the removal of lymphoid tissue.

It has long been known that infection plays an important role in the development of respiratory allergy and that children of allergic parents or those with food sensitization or eczema, who are subject to upper respiratory infections, should be considered as allergic suspects, and prompt corrective measures instituted. Especially is this true of children subject to frequent winter colds, in whom cough and sometimes wheezing is a prominent if transient symptom. In the very young and in early adult life, lymphoid tissue in the pharynx and nasopharynx is the primary focus of these infections. Later in life when the nose has become filled with polyps and the sinuses and bronchial mucosa are chronically infected, the results of surgery, chemotherapy, and the administration of antibiotics are much less satisfactory. In children complete surgical removal of tonsils and adenoids, together with protection against airborne or environmental pollens, dusts, and danders often effect a cure. In others the cough and wheezing recur a few months or a year later.

When asthmatic symptoms of a child improve following operation and recur at some later date, the otolaryngologist rarely has any difficulty in finding more infected tissue to remove. Through the accident of a shortage of beds, particularly free beds, we were forced to postpone operation on these and patients with other maladies. This led to the establishment of a radium clinic in the otolaryngological dispensary, so that at least their adenoids could be treated. To prevent overexposure to the doctors, the radium treatments were limited to the nasopharynx. For several years an average of 150 patients a month were treated. Among them were many with asthmatic bronchitis waiting for operation, and others in whom

the asthmatic symptoms had recurred following removal of tonsils and adenoids. Sometimes following the second, but usually about a month after the third irradiation, the parents would report marked improvement or complete disappearance of asthmatic symptoms. These reports were so positive and frequent that a coordinated study was begun in 1943 by the pediatric, allergy and nose and throat departments. A full and detailed report will soon be published, but I can say now it is an established fact that the results following irradiation of the nasopharynx alone are as good and often better than those following operative removal of tonsils and adenoids. This has given us proof that the greater number of upper respiratory infections have as their focal point the nasopharynx. All children having these treatments in the nasopharynx should be examined at least once a year, and if lymphoid tissue recurs, additional treatments should be given. Irradiation with the nasopharyngeal radon or radium applicator is a method of treatment that can be used on patients of all ages to remove lymphoid tissue in locations inaccessible to ordinary surgical measures. It is effective, safe, painless, inexpensive and has proved particularly valuable for prevention of certain ear, sinus and bronchial conditions in children.

The technic of examination with the nasopharyngoscope and treatment with the radium applicator is simple, even in the case of children of school age. After a few preliminary questions about the symptoms, we select the side of the nose that is least obstructed, and by spraying lightly with five per cent butyn begin the anesthetization. We then take a careful history, test the hearing with voice and tuning forks, and make a routine examination of the tympanic membranes and the upper air passages. An audiometric test, if indicated, is made later in a soundproof room. At intervals the examination is interrupted and the lower half of the septum, the inferior turbinate and the posterior wall of the nasopharynx are further anesthetized with a small cotton-tipped applicator, moistened with 20 per cent cocaine. By thus prolonging the anesthetization period the minimum amount of cocaine can be used, and at the conclusion of the routine examination we can at once proceed to pass the nasopharyngoscope. To make a satisfactory examination with the nasopharyngoscope, all thick mucus on the floor of the nose and in the nasopharynx must be removed with a suction tip. In young or very nervous children, it is impossible to examine the nasopharynx with a nasopharyngoscope under local anesthesia. Even if the head is held firmly, the excess mucus that results from crying obscures the view. In these patients we must decide whether the nasopharyn-

goscopic examination is important enough to justify general anesthesia or whether we should treat them on the basis of history and such examinations as we can make without upsetting the child psychologically and thus rendering all future examinations and treatments even more difficult. If irradiation of the nasopharynx is indicated by the history, we treat these children without examination, since we know from 20 years' experience that if properly used, the radium applicator can do no harm.

I have found it easier to keep the radium-containing chamber in contact with the tissue to be removed if the patient lies on a couch. Especially is this true when the pharyngeal orifice of the eustachian tube is being treated. When irradiating the right eustachian orifice the head is turned to the left, and vice versa. For protection of the doctor and the office personnel the applicator should be left in the lead cylinder until everything is in readiness for its insertion into the nasopharynx. If many treatments are being given each day, we must realize that the applicator is out of the lead much of the time. This exposes our own office force and even those in other offices separated by a partition who are within a few feet of the applicator. To guard against this constant danger distance is the best protection, since the intensity of the radiation varies inversely with the square of the distance. At 20 feet the radiation is 1/400 of that at one foot. It is of the utmost importance for the radium to be stored and the treatments to be given at least 20 feet from those who are daily exposed to its effects. The two-inch lead cylinder that comes with the applicator is intended to make transportation practicable, but for storage in an office the lead should be at least six inches in thickness. A cylinder of this size and weight should be mounted on a table that can be wheeled from room to room.

The tissue reactions and the therapeutic value of a radium treatment depend entirely on the absorption of beta and gamma rays. All beta rays emitted by the 50 mg. monel metal applicator are absorbed by tissues in the nasopharynx, and approximately 75 per cent are absorbed in the first three millimeters. This is another reason for removing greatly enlarged adenoids at operation and irradiating the relatively small amount that is left, rather than treating with radium alone. Every variety of cell in the body has a specific range of sensitiveness to beta and gamma rays. The sensitiveness of cells depends on their life cycle and mitotic activity. In adenoid tissue the germinal center cells are much more sensitive than the mature lymphocytes, and their sensitiveness to irradiation varies with the

degree of mitotic activity at the time of the treatment. For this reason the response of the adenoids to irradiation is often more satisfactory in children than in adults. As we all know, a heavy dosage is used to irradiate a malignant growth, since the object is to injure the cells so seriously that they will never recover. The dosage used in treating hypertrophied lymphoid tissue, however, is just enough to stop mitosis in the germinal centers. As the mature lymphocytes complete their life cycle and are discarded, no new ones are being formed to replace them, and the entire mass gradually decreases in size leaving only the fibrous framework. With the dosage we use, the degree of tissue injury is small and some of the germinal center cells may recover. If they do, lymphoid tissue will eventually regenerate, in which case further irradiation may be necessary.

In treating the nasopharynx it is always essential to use a dosage that we know will not injure adjacent normal structures. We advise three treatments of 8½ minutes on each side, with the 50 mg. monel metal radium applicator in direct contact with the tissue to be removed; then a wait of 30 to 60 days after the third treatment before considering further irradiation. The object of the treatments is to remove the particular lymphoid tissue which is causing the patient's malady, not to remove all lymphoid tissue in the nasopharynx. If symptoms do not return, it is unnecessary to give further radium treatments, but if needed they can be given with perfect safety. During the war approximately 25,000 treatments were given with the monel metal radium applicator by medical officers of the Army Air Forces and at the New London Submarine Base, in order to prevent recurrent aerotitis and thus conserve manpower. The average result was 90 per cent effective. Not a single instance of radium burn or radium poisoning, with a drop in the white count, has been reported. The author has given treatments with the nasopharyngeal applicator almost daily for 20 years and has suffered no ill effects. Years of experience together with histologic study of adenoids irradiated and then removed surgically at varying intervals have shown that 1 gram 25.5 seconds, or 8.5 minutes on each side of the nasopharynx at intervals of two weeks, is the safe and most effective dosage for the 50 mg. monel metal radium applicator. The only requirements are an accurate examination with the nasopharyngoscope to establish the indication for radium treatment, placing the applicator so that the side, not the end, of the radium-containing chamber is in contact with the tissue to be treated, and finally the greatest care to time each treatment accurately.

In closing I wish again to emphasize the great value of irradiation in otolaryngology, if intelligently and carefully used. May I solemnly urge those of you who have an applicator, or intend to use one in your practice, to surround yourselves and your office personnel with protection essential to its safe employment.

THE JOHNS HOPKINS HOSPITAL.

LXXI

INCIDENCE OF MALIGNANT NEOPLASTIC DISEASE OF THE HEAD AND NECK

A STATISTICAL COMPARISON

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The interpretation of statistical data is always suspect. With the best of intentions, the investigator may read into his figures conclusions which do not stand the test of comparison. Where all conditions are equal, comparisons should show a similarity in result. Where results differ, one must examine the situations upon which the tests were made for variations to account for the unlike results.

The last statistical survey of malignant tumors of the head and neck recorded in the Department of Laryngology, Rhinology, and Otology of the University of Illinois College of Medicine covered the period July 1, 1930, to June 30, 1937, inclusive.[1] Two hundred forty-nine cases were diagnosed as cancer and confirmed by histologic examination. In the period July 1, 1937, to December 31, 1945, an additional 553 cases were diagnosed as malignant neoplastic disease and in each case the diagnosis was confirmed by histologic examination. Again we emphasize the point made by Fabricant that the diagnosis of malignancy in this department is based upon biopsy done at the institution, with the specimens examined histologically by competent clinicians and pathologists. In no case has a diagnosis of malignant neoplastic disease been based on clinical interpretation alone. Eighty-five of our patients had incomplete histories or lacked certain information we deemed essential to a consideration of the problem of cancer and these cases were therefore eliminated from this report.

In contrast to the period of the last survey when a world-wide economic crisis tended to increase the patient flow into the free clinic, the present survey covers a period not only of increasing economic independence, but also of a decreased patient source because of the

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segregation of a considerable proportion of the population in the armed forces.

YEAR	NEW PATIENTS
July 1, 1937, to Dec. 31, 1937	1289
Jan. 1, 1938, to Dec. 31, 1938	2871
Jan. 1, 1939, to Dec. 31, 1939	2608
Jan. 1, 1940, to Dec. 31, 1940	2177
Jan. 1, 1941, to Dec. 31, 1941	1954
Jan. 1, 1942, to Dec. 31, 1942	1846
Jan. 1, 1943, to Dec. 31, 1943	1561
Jan. 1, 1944, to Dec. 31, 1944	1543
Jan. 1, 1945, to Dec. 31, 1945	1917

While the general average amounts to about 2100 patients each year, the high and low vary from this by more than 600 patients since the pre-war high of 2871 dropped to 1543 during the war. On the 17,766 new patients seen, over 2400 biopsies were made by members of the department.

It is interesting to note that despite a progressive decline in the number of new patients seen, there has been both a real and a relative increase in the number of malignant tumors diagnosed. There were 23 in the last half of 1937, 41 in 1938, 50 in 1939, 46 in 1940, 39 in 1941, 43 in 1942, 69 in 1943, 79 in 1944 and 78 in 1945.

The ratio of biopsies showing malignant tumors to total biopsies was 28.05 per cent in the last half of 1937, 22.40 per cent in 1938, 17.36 per cent in 1939, 16.25 per cent in 1940, 13.22 per cent in 1941, 14.47 per cent in 1942, 31.65 per cent in 1943, 25.82 per cent in 1944 and 22.99 per cent in 1945.

We note a marked rise in the ratio of malignant tumors in 1943 and subsequent to that date. The cause for this has been determined. In 1942 a Tumor Clinic was established at the University of Illinois and by 1943 it was functioning sufficiently well to attract persons with malignant neoplastic disease. The Tumor Clinic has proved a greater factor in cancer statistics than did our Bronchoesophagology Clinic which began to function about ten years ago. The tendency for the percentage incidence of malignancy compared to total biopsies to drop will probably become more marked in our department since the present attitude is to section all specimens with variations from the normal despite apparent clinical benignancy.

ANNUAL CANCER INCIDENCE

YEAR	INCIDENCE PERCENTAGE
July 1, 1937, to Dec. 31, 1937	1.78
Jan. 1, 1938, to Dec. 31, 1938	1.43
Jan. 1, 1939, to Dec. 31, 1939	1.92
Jan. 1, 1940, to Dec. 31, 1940	2.21
Jan. 1, 1941, to Dec. 31, 1941	1.99
Jan. 1, 1942, to Dec. 31, 1942	2.33
Jan. 1, 1943, to Dec. 31, 1943	4.42
Jan. 1, 1944, to Dec. 31, 1944	5.12
Jan. 1, 1945, to Dec. 31, 1945	4.07

While one notes an incidence percentage consistent with the finding of the previous survey in the period through 1942, the marked increase in the succeeding period is again due to the effect of the Tumor Clinic in determining the general type of patient applying to this institution.

The seven-year survey of Fabricant involved 18,384 new patients and revealed a malignant neoplastic disease incidence of 1.35 per cent. Our eight and a half year survey concerned 17,766 new patients with a cancer incidence of 2.63 per cent. The total incidence for the fifteen and a half year period based on 36,150 new patients was 1.98 per cent. Since this figure covers a period representing both extremes of the economic state and excludes from the general population only a part of those in the low incidence age group, it can be accepted as the approximate norm.

The sex distribution revealed 87.39 per cent occurring in males and 12.61 per cent occurring in females. This corresponds exactly to the findings of Fabricant and is acceptably similar to those of Boot.[2] We, therefore, confirm their findings that malignant tumors of the head and neck occur seven times as frequently in men as they do in women. The youngest male was 16 years of age; the oldest 89. The age span for males was 73 years. The youngest female was 4 years of age; the oldest 80. The age span for females was 76 years. The average age for the occurrence of malignant neoplastic disease was 58.7 years in males and 49.2 years in females. Only in the first and second decade did the incidence of cancer in the female exceed that which occurred in the male.

The incidence of malignant neoplastic disease according to age reveals a smooth curve which approximately doubled in each decade to the fifth and then increased 150 per cent to reach a peak in the

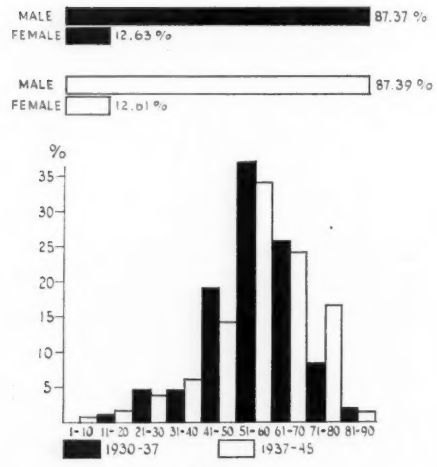

Fig. 1.

sixth decade. It dropped one-third in the seventh decade and to one-half in the eighth decade. The percentage incidence of the ninth and second decades was equal. The findings in the two surveys are not materially out of line. The difference is probably due to the better distribution obtained from the increased number of patients in the second group. The chart (Fig. 1) graphically indicates the sex and age distribution of malignant neoplastic disease for the two surveys.

The following comparative tabulation represents the anatomic site and the number of cases in the two surveys:

	NUMBER OF CASES		
ANATOMICAL SITE	1930-37	1937-45	TOTAL
1. Larynx	57	80	137
2. Tongue	22	20	42
3. Esophagus	29	93	122
4. Neck	18	8	26
5. Tonsil	10	12	22
6. Bronchus	20	69	89
7. Epiglottis	6	16	22
8. Nose	23	32	55
9. Mouth	7	16	23
10. Pharynx	8	54	62
11. Jaw	5	2	7
12. Ear	8	15	23
13. Thyroid	1	1	2
14. Antrum	7	12	19

ANATOMICAL SITE	NUMBER OF CASES 1930-37	1937-45	TOTAL
15. Cheek	2	2	4
16. Face	5	0	5
17. Lip	2	4	6
18. Gingiva	4	3	7
19. Lung	3	3	6
20. Eye and orbit	8	2	10
21. Frontal sinus	1	1	2
22. Submaxillary gland	1	0	1
23. Parotid gland	1	1	2
24. Trachea	1	4	5
25. Other sites	0	18	18
	249	468	717

The 468 malignant tumors considered in this group were histopathologically diagnosed as various "grades" of the following tumor types:

Squamous cell carcinoma	281
Epidermoid carcinoma	77
Adenocarcinoma	21
Transitional cell carcinoma	18
Basal cell carcinoma	17
Bronchogenic carcinoma	13
Undifferentiated cell carcinoma	10
Lymphosarcoma	6
Fibrosarcoma	6
Round cell carcinoma	3
Lympho-epithelioma	3
Cylindrical cell carcinoma	2
Reticulum cell sarcoma	2
Mixed tumor	1
Hodgkin's granuloma	1
Carcinosarcoma	1
Osteogenic sarcoma	1
Fibromyxosarcoma	1
Neurofibrosarcoma	1
Chordoma	1
Malignant melanoma	1
Adamantinoma	1

The 1930-37 report listed the squamous cell type of carcinoma as comprising 70 per cent of the group. Our figures reveal 60.04 per cent to be squamous cell carcinoma and 16.45 per cent epidermoid carcinoma. The various sarcomata had a 3.85 per cent incidence.

Fabricant listed the order of predilection of malignant tumors in reference to site as: 1) larynx; 2) nose and paranasal sinuses; 3) esophagus; 4) tongue; 5) bronchi. Our record indicated the greatest incidence in the esophagus with the larynx, bronchi, pharynx, nose and paranasal sinuses and tongue following in that order. The

combined figures reveal 137 cases involving the larynx, 122 in the esophagus, 89 in the bronchi, 76 in the nose and paranasal sinuses, 62 in the pharynx and 42 in the tongue.

The site incidence of the two reports compares favorably with that of Lederer, who surveyed the malignant tumors of the head and neck for the ten years preceeding Fabricant's report. His grouping of sites differs from those in the two subsequent reports and does not lend itself to exact comparison.[3]

CONCLUSIONS

A statistical survey of malignant neoplastic disease about the head and neck as seen in the Department of Laryngology, Rhinology, and Otology at the University of Illinois College of Medicine during an eight and one-half year period (1937-45), when compared and consolidated with a similar survey for the seven previous years, established the following facts.

1. Malignant neoplastic disease occurs most frequently in the sixth decade with the seventh next in order.

2. Malignant tumors occur seven times more frequently in males than in females.

3. The age span for cancer incidence is approximately the same for the two sexes, but that of the male begins about nine years later than that of the female.

4. Most tumors are of the squamous cell type.

5. Carcinoma of the larynx is closely followed in incidence by carcinoma of the esophagus and the two make up more than one-third of the malignant tumors of the head and neck.

6. The presence of a tumor clinic in an institution will tend to increase the case incidence of malignant neoplastic disease.

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LXXII

CHEMICAL BURNS OF THE ESOPHAGUS

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Chemical burns of the esophagus are common, if not constant, problems confronting most otolaryngologists, pediatricians and general practitioners. Only by the very earliest and closest cooperation between these physicians can sequelae be averted. Usually sequelae can be prevented by comparatively easy measures. On the other hand, a clinical cure of that morbid condition, cicatricial atresia of the esophagus, is too often impossible except by means of formidable surgical procedures.

Incidence and Chemicals. The clinical records of all patients treated in the University of Oregon Hospitals for chemical burns of the esophagus from February 1, 1931, to February 1, 1946, were studied by the author. The former date was selected for the inception of this review because the Unit System according to the Standard Nomenclature was instituted at that time. All previous records are filed under a different system.

During this period 34 patients were hospitalized for chemical burns of the esophagus. There are three other patients with lye burns undergoing treatment at the present time. Of course, a far greater number of patients were treated for the swallowing of chemical agents but many did not show any clinical evidence of esophageal damage.

The chemicals responsible for the burns of the esophagus were as follows:

From the Department of Otolaryngology, University of Oregon Medical School Hospitals and Clinics.

Presented to classes attending the postgraduate courses for General Practitioners 1945-46.

TABLE 1

THE CHEMICALS CAUSING BURNS OF THE ESOPHAGUS TREATED AT THE UNIVERSITY OF OREGON OVER A 15-YEAR PERIOD.

	PATIENTS	
CHEMICAL	NO.	PER CENT*
Lye	22	64
Lysol	2	6
Bichloride Mercury	2	6
Phenol	1	3
Iodine	1	3
Formaldehyde	1	3
Silver Salt	1	3
Sulphuric Acid	1	3
Hydrochloric Acid	1	3
Lactic Acid	1	3
Clorox (Halogen)	1	3
Total	34	100

*Percentages tabulated in whole numbers only.[1]

It is quite evident from the above table that lye was responsible for most of the chemical burns of the esophagus. This observation has been common knowledge for many years as evidenced by the voluminosity of the literature[2] on this subject. If lye was eliminated as a household agent, chemical burns of the esophagus would be uncommon and would in most instances be the result of attempted suicide.[3]

The greatest contribution which has been made to date towards a correction of the misuse of lye is the legislation of a federal law providing for proper labeling of packages of household lye and other poisons. This law was passed in 1927, mainly through the efforts of Jackson and his many friends and co-workers in otolaryngology. Since the clinical records of this institution prior to this date are not available for a statistical study, the effect of this law in Oregon could not be determined. Nevertheless, several authors[4, 5] reported a reduction of 50 to 90 per cent in the number of lye burns in the states of Pennsylvania, Florida and Colorado. It is probably safe to assume that there has been a similar decrease in the number of these burns

in this state. However, these lye burns are still, even to-day, too frequently encountered.

Other chemicals mentioned in the literature[6-11] as causing burns of the esophagus are nitric, acetic, chromic and oxalic acids, copper sulphate, ammonia, wood-staining compounds, caustic dyes and chloroform.

By far the greatest number of chemical burns of the esophagus occur in children, as is shown by Table 2.

TABLE 2

THE AGE-GROUPS OF THE PATIENTS WITH ESOPHAGEAL BURNS ACCORDING TO SEX, WHEN BURNED AND WHEN INITIAL TREATMENT WAS REQUESTED

AGE GROUPS IN YEARS	WHEN BURNED				REQUESTED TREATMENT			
	MALE		FEMALE		MALE		FEMALE	
	NO.	PER CENT*	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
1 to 10	20	59	7	20	18	53	6	17
11 to 20	2	6			3	9		
21 to 30	2	6			2	6		
31 to 40	1	3	1	3	1	3	1	3
41 to 50			1	3				
51 to 60					1	3	1	3
61 to 70							1	3
Total	25	74	9	26	25	74	9	26

*Percentages tabled in whole numbers only.[1]

In other words, 27 out of 34 patients, or 79 per cent, were children under 10 years of age.

The only apparent reason why 74 per cent of the patients were males is that boys are more active and mischievous than girls and therefore more apt to seek the contaminant. On the other hand, in Korea[68] the majority of the patients are females who drink lye with suicidal intent.

Examination of Table 2 also reveals the fact that although an esophagus may be burnt and some dysphagia result, the patient may not request treatment until years later, at which time the stricture is usually blocked by a foreign body.

Reports[12, 13] show that majority of chemical burns of the esophagus are due to ignorance and carelessness on the part of parents. The data presented in Table 3 was collected from the records containing any information appertaining to the whereabouts of the chemicals at the time the children were contaminated.

TABLE 3

THE SOURCE OF THE CHEMICALS CAUSING BURNS OF THE ESOPHAGUS. NO INFORMATION RECORDED ON 21, OR 62 PER CENT, OF THE PATIENTS.

SOURCE OF CHEMICAL	NUMBER OF PATIENTS
Lye in Yard	4
Lye in Medicine Cabinet	3
Lye on Floor of Home	2
Lye in Pantry	2
Lye in Milk Bottle	1
Mother Gave Infant Teaspoonful of Lactic Acid Full Strength (U.S.P. 87.5%) instead of Elixir Phenobarbital	1

Symptomatology. The symptomatology of an esophageal burn is contingent upon the severity of the esophageal obstruction but is not always prognosticative of the final degree of stricture. In other words, the swelling of the acute burn may be so severe within the first week as to result in complete obstruction; such a case was described by Lederer.[14] Next there is very frequently a dangerous asymptomatic period, or an improvement in the symptoms, commencing concomitant with the subsidence of the acute inflammatory reaction, usually in one to two weeks, and ending with the onset of stenosis of the scarred area, usually in four to six weeks.

According to Vinson,[15] in acid and alkali burns of the esophagus, the mouth and pharynx are always involved and cause the major portion of the primary discomfort but pain, fever, dysphagia, acidosis from dehydration and acute starvation are the outstanding symptoms. When the acute inflammatory reaction subsides (one to two weeks), the patient is able to swallow soft foods and liquids for a month or six weeks at which time contraction of scar tissue in the esophagus increases the dysphagia, so that the patient may be unable to swallow

even liquids. When the stricture closes the esophagus completely, regurgitation and expectoration of frothy mucus are continuous.

It was impossible to determine with any accuracy the absolute or relative frequency of occurrence of various symptoms in the patients treated in this institution for lye burns of the esophagus, since the clinical records were inconsistent in furnishing both positive and negative information concerning each of the indicated symptoms shown in Table 4.

TABLE 4

THE FREQUENCY OF OCCURRENCE OF DIFFERENT SYMPTOMS RECORDED IN THE CLINICAL RECORDS OF 22 PATIENTS TREATED FOR LYE BURNS OF THE ESOPHAGUS AT THE UNIVERSITY OF OREGON OVER A 15-YEAR PERIOD.

SYMPTOM	NUMBER OF PATIENTS WITH SYMPTOM PRESENT	TOTAL UNIT RECORDS WITH ANY NOTATION OF THIS SYMPTOM
Dysphagia		13 (58%)
(a) Unable to swallow liquids	4	
(b) Unable to swallow soft foods	7	
(c) Unable to swallow general diet	2	
Odynphagia	7	7 (32%)
Regurgitation		11 (50%)
(a) Bloody	4	
(b) Not bloody	7	
Weight Loss	5	5 (23%)

Clinical Signs and Pathology. Tucker[17,18] stated that in esophageal stenosis mirror examination of the larynx will show the pyriform sinuses filled with frothy secretion (Jackson's sign). Another sign frequently observed but not commonly mentioned in the literature is stridor which is due to pressure of the glutted esophagus above the stricture on the trachea.

Of the 22 lye burns of the esophagus, 9 or 41 per cent, were late stricture cases in which the early lesions were not recorded. In the remaining 13 patients, or 59 per cent, the frequency of occurrence of the lesions is shown in the following table:

TABLE 5

THE FREQUENCY OF OCCURRENCE OF LESIONS IN 13 PATIENTS WITH ACUTE LYE BURNS OF THE ESOPHAGUS.

LESION	FREQUENCY OF OCCURRENCE NO.	PER CENT
Inflammation or ulceration of esophagus	13	100
Inflammation or ulceration of esophagus and ulceration of pharynx	7	54
Inflammation or ulceration of esophagus and inflammation of lips and ulceration of tongue	5	38
Inflammation or ulceration of esophagus and inflammation of tongue and pharynx and ulceration of mouth	4	31
Inflammation or ulceration of esophagus and inflammation of soft palate and epiglottis and ulceration of lips	2	15
Inflammation or ulceration of esophagus and inflammation of arytenoids and ulceration of the soft palate and tonsils	1	8

A lye burn at 24 hours has the following appearance: The mucosa is severely swollen and frequently eroded. The ulcers are covered with a brownish-grey exudate or slough. At 7 to 14 days, depending upon the severity of the burn, there may be considerable granulation tissue which bleeds readily. At six weeks many of the granulations are replaced by fibrous tissue.

According to Jackson[19] inflammation and later strictures of the esophagus resulting from chemical burns are most frequently found at the level of the anatomic and physiologic narrowings, that is, most frequently at the level of the crossing of the left bronchus, next, in the region of the cricopharyngeus and, last, at the hiatal level.

Mosher[20] mentioned the frequency of stricture at the hiatus or at the beginning of the liver tunnel, due to the delay of the caustics (and food) at this point.

Abel[6] stated that a simple stricture is present in about 60 per cent of the cases and that in multiple strictures the lower stricture is usually the tightest.

Jackson[19] contended that the strictures are eccentric rather than annular but MacMillan[21] found that in 75 per cent of the cases there was a tubular stricture.

Examination of Table 6 shows that it is a wise policy to consider a patient with a chemical burn of the mouth and pharynx as having an esophageal burn until it is proven otherwise. The severity of the oral lesion, however, is no index of the seriousness of the esophageal damage, since a concentrated caustic solution causes a severe oral lesion but also immediate irritation so that the child is instantly warned and spits out the contaminant, whereas a diluted solution may be swallowed in rather large quantities before the child recognizes his danger.

TABLE 6

A DICHOTOMOUS CLASSIFICATION OF THE LOCATION OF CHEMICAL LESIONS IN 34 PATIENTS ON ADMISSON TO DOERNBECHER AND MULTNOMAH HOSPITALS.

		LESIONS PRESENT IN ESOPHAGUS			
	NO. OF	PRESENT IN MOUTH OR PHARYNX		NOT PRESENT IN MOUTH OR PHARYNX	
CHEMICAL	CASES	NO.	PER CENT	NO.	PER CENT
Lye	22	13	59	9*	41*
Lysol	2	2	100		
Bichloride Mercury	2	2	100		
Phenol	1	1	100		
Iodine	1	1	100		
Formaldehyde	1	1	100		
Silver Salt	1	1	100		
Sulphuric Acid	1	1	100		
Hydrochloric Acid	1	1	100		
Lactic Acid	1	1	100		
Clorox	1	1	100		

*Late stricture cases in which the early lesions were not recorded.

The esophageal lesions due to the following agents were of a diffuse erythematous nature and did not result in any stricture: lysol, phenol, iodine, formaldehyde, hydrochloric acid and clorox. Carbolic acid[69] results in death from toxic absorption from the stomach and patients who recover seldom develop esophageal stricture.

A white male, aged 40, swallowed some silver salts in order to commit suicide and falsified his history. This mendacious individual died 12 hours later and the postmortem findings were severe destruction of the esophageal mucosa with extensive deposits of clumps of brown pigment and edema of the remaining wall.

The bichloride of mercury swallowed to commit suicide also resulted in death and localized areas of necrosis at the points of lodgement of the pills.

The sulphuric acid was swallowed by a white boy at the age of two years, and three years later he was still being treated for esophageal stenosis at both the cricopharyngeus and at the hiatus.

Trainer et al[23] reported the lactic acid burn in detail. A male infant, two weeks of age, received a teaspoonful of lactic acid (U. S. P. 87.5 per cent) instead of elixir phenobarbital. He died at the age of seven months with esophageal strictures complicated by an esophageal perforation and aspiration pneumonia. At necropsy two strictures of the esophagus were found, one just below the level of the thyroid cartilage and the other 2.4 cm. inferior to the first. A small wad of folded paper was removed from the lumen between the strictures. A perforation of the esophagus, 2 mm. in diameter, was present midway between the strictures and extended posteriorly into the mediastinum. There was a greenish discoloration of the mediastinal tissues above and below the perforation for a distance of 5 mm. A section through the perforation of the mucosa showed not only necrosis of the mucosa and submucosa but also well-defined, acute, exudative inflammation which spread into the submucosa and muscularis. Most of the wandering cells were neutrophilic granulocytes, the remainder being monocytes and lymphocytes.

A white male, aged two years, swallowed lye and died two months 27 days later with brain abscesses of both temporal lobes.[70] Postmortem examination showed a marked narrowing of the esophagus at about the level of the cricoid cartilage, or about 3.5 cm. below the arytenoid cartilages. The total circumference of the mucosal surfaces of the constriction was only 8 mm. Beginning 7 cm. below the arytenoids to within 3 cm. of the cardia of the stomach the mucous membrane had sloughed out resulting in extensive ulceration. The remaining layers of the esophagus beneath the ulcer were swollen. Below the ulceration the esophagus again assumed a normal appearance except for the disappearance of the usual rugae. Just beneath and anterior to the right main stem bronchus a large lymph node measuring 2 cm. by 1 cm. was found. On sectioning this large node a

yellowish-green material of purulent character escaped from its central portion. Other than this node, there was no evidence of any extension of inflammation beyond the esophagus into any of the mediastinal tissues. The blood vessels over the adventitial portion of the esophagus were slightly injected. A gastrostomy wound was present.

Diagnosis and Treatment. In the differential diagnosis cardiospasm and cancer are two of the most common conditions one must differentiate from benign stricture due to chemicals. The secondary inflammation above a cardiospasm may lead to a true cicatricial stenosis. There are many causes other than chemical burns responsible for fibrotic strictures, viz. typhoid fever, vomiting during pregnancy, scarlet fever, diphtheria, prolonged sojourn of foreign bodies, peptic ulcer of the esophagus, ulcer associated with diaphragmatic hernia, mediastinitis of nonspecific or tuberculous origin, spontaneous rupture of the lower part of the esophagus,[24] lues, pyogenic conditions, wounds, burns from hot foods (and in England hot water or tea) and hysterical dysphagia.

There is a great diversity of opinion as to the best method of treatment of esophageal burns and strictures. Each esophageal burn is a problem per se and accordingly there is some variation in treatment. Nevertheless, there must be a standard course of action to be followed in each burn in order to prevent atresia and all its piteous sequelae. At the present time residents in the University of Oregon Hospitals are instructed to carry out the following procedures in the treatment of all acute esophageal burns:

1. Immediate neutralization of the poison.

2. Immediate swallowing of a size D twisted (not braided) silk thread on completion of Procedure 1.

3. Treatment to avoid dehydration and starvation.

4. Consultation with an otolaryngologist within 24 hours.

5. Barium swallow under fluoroscopy and with flat plates as soon as the initial fever subsides, usually in 7 to 10 days.

6. Esophagoscopy after determination of the site and degree of obstruction by Procedure 5.

7. Following the esophagoscopy bouginage up to 45 French in an adult with mercury bougies of the Salzer or Bokay types, carried out once or twice weekly or less often depending upon the stricture's

reaction to bouginage and the patient's ability to swallow. Bouginage is performed over a period of six months to two years depending upon the results.

8. If frequent bouginage is unsuccessful, that is, if the child is in danger of becoming malnourished with a retardation in normal development, a gastrostomy is to be performed, the esophagus placed at rest and the stricture dilated in the retrograde manner advocated by Tucker.

Caustic alkalies (lye, 95 per cent sodium hydroxide) can be neutralized with vinegar and caustic acids with sodium bicarbonate. When in doubt about the proper antidote, examine the label on the container.

Vinson[15, 16] recommended the administration of large amounts of olive oil and parenteral fluids as soon as possible after lye has been swallowed.

Lower[25] and Heatly[26] advised bismuth subnitrate, one gram, dry, on the tongue every four hours, to relieve the discomfort of the acute inflammatory reaction.

The medical treatment of esophageal strictures is of little value at the present time and will most likely remain so until a really effective medicament for the destruction of fibrous tissue is discovered. Even then, the use of such medication would probably be fraught with danger. Abel[6] stated that the most potent drugs for the diminution of fibrous tissue are sulphur and iodine. Atropine and morphine are useful antispasmodic drugs.

It is possible that lye penetrates tissues so rapidly that the present method of neutralization is useless. This possibility could be investigated experimentally.

The patient should be given a twisted (not braided) silk thread to swallow as soon as neutralization has been completed. Some authors advise a delay of six to ten days in swallowing the string until there is a subsidence in the acute swelling. This thread is left in place many weeks until all danger of atresia has vanished and the esophagus has responded well to treatment.

Tucker[17, 18] suggested a No. 15 button-hole twisted silk thread for use in very small strictures and as soon as this latter thread has successfully passed the stricture, a No. 4 Pearsal's twisted silk thread is attached. A bass or trout fishing line is very satisfactory for the latter purpose.

In infants a small rubber catheter is used to push the string through the nasal passage into the oropharynx where the string is observed by depressing the tongue. The catheter is withdrawn and the thread, starting with the distal end, is wrapped around a bobbin secured with adhesive tape to the neck. Then the nurse can intermittently loosen the string, especially just prior to mealtime, and it will eventually be swallowed although it may take many days, much patience and being regurgitated many times. Swallowing water may be of aid in getting the string through the stricture. Peristalsis gradually pulls the thread through the intestinal tract and a segment can be cut off after each bowel movement. After the thread becomes anchored in the intestinal tract, the pull of the string on the side of the nose may be considerable and quite annoying to the patient. The tension of the string can be alleviated temporarily by feeding a few more centimeters to the patient.

Von Acher recommended the attachment of perforated shots or steel balls to the distal end of the string.

Moersch[27] and Lower[25] stated that the attachment of a small shot to the end of the thread to facilitate deglutition should be avoided since it often defeats its own purpose by plugging whatever lumen is left.

Tucker[17, 18] found that the unknotted, slightly frayed end of the string is best.

Vinson[15, 16] believes that a thread will pass through an obstruction and dilatation can be accomplished even when a patient is unable to swallow liquids and that if all patients were instructed to swallow a thread before the esophagus has become completely obstructed, gastrostomy would never be required.

Dehydration and starvation must be combatted by oral and parenteral fluids.

Walley[28] advised the general practitioner to get the patient in the care of an otolaryngologist as quickly as possible.

Fluoroscopic examination by swallowing barium, or in the event of a very small stricture a more fluid medium such as lipiodol, supplemented by films may be of use in determining the number, level, length and severity of the strictures.

Vinson[15, 16] stated that a stricture may not be demonstrated on roentgenoscopic study and that in a benign stricture of known etiology, observation of the passage of barium through the esophagus under the fluoroscope is seldom necessary.

In a child who refuses to swallow the contrast mixture, a soft rubber catheter may be passed through the nose and the opaque substance injected into the upper esophagus as employed by Pancoast in Tucker's clinic.[17, 18]

Esophagoscopy is by no means easy in the presence of a stricture, especially if there are multiple strictures. The examination is greatly facilitated if a string has been swallowed, since it can be used as a guide, and there is much less danger of perforating the esophageal wall. In the presence of acute swelling and granulation tissue bleeding readily occurs. During the late stage of scar tissue constriction the esophagus is dilated above the stricture and frequently glutted with food and mucus and the condition complicated by secondary infection, swelling and spasm.

There is considerable controversy as to the indications for esophagoscopy. Abel[6] stated that dilatation of a simple stricture of the esophagus should always be performed under direct vision by means of an esophagoscope.

Lower[25] believed esophagoscopy should always be done before any method of treatment is instituted.

Hoag[29, 30] advised immediate penetration of the stricture by use of an esophagoscope to prevent complete and permanent obliteration of the lumen and to allow feeding if a gastrostomy is to be avoided.

On the other hand, Jesberg[31] emphasized the fact that early instrumentation in a badly inflamed and excoriated esophagus is a very dangerous matter and that putting a tube into such an esophagus is sure to increase the inflammation. In his experience at least six children died because instrumentation was done too early.

Vinson[15, 16] stated that esophagoscopy is especially contraindicated in children who have acquired burns of the esophagus from lye, because the examination is uncomfortable, serves no useful purpose and increases the risk of treatment.

There are numerous possible methods of treatment of esophageal stricture or atresia. Some of the most commonly used methods, both good and bad, are: blind bouginage, fluoroscopic bouginage, passage of dilating instruments over a taut string, esophagoscopy with direct bouginage, gastrostomy with continuous string and retrograde bouginage, continuous indwelling tubes (e. g., Levine), dilatation of the esophagus with soft rubber, mercury- or shot-

filled bougies (another form of blind bouginage but pressure is never used), combined peroral and retrograde esophagoscopy with or without double plane fluoroscopic guidance, internal esophagotomy, autodilatation, electrolysis, open mediastinotomy and exposure of the stricture, resection of the esophageal stricture with end-to-end anastomosis, side-to-side anastomosis of the esophagus and stomach, construction of an artificial esophagus, plastic operation and external esophagotomy.[76]

Vinson recommended postponement of the dilatation of the stricture until the patient begins to notice difficulty in swallowing liquids.

Montgomery[32] stated that the secondary contraction of scar tissue usually reduces the lumen in six weeks to a point where liquids cannot be swallowed and it is necessary at this time to begin dilatations.

Treatment has advanced far since the day of Trousseau's blind bouginage and Home's[33] blind caustic bouginage.

Blind bouginage cannot be too strongly condemned since the mortality rate is at best around 40 per cent.

Mosher[34] used fluoroscopic bouginage in selected cases in the dilatation of small strictures of the esophagus but admitted it is always attended with risk.

Many authors[35-39] recommend the use of rubber bougies filled with mercury or lead shot. Initially in this institution these bougies were passed daily commencing as soon as the patient arrived at the hospital. However, it was found that the reaction of a patient's acute burn to bouginage was quite severe as evidenced by pain, fever and bleeding. This experience forced us to modify our procedure so that now bouginage is delayed until the temperature becomes normal, the acute swelling subsides and granulation tissue has had an opportunity to begin to cover over (but not contract) the erosion, that is, in seven to ten days. These mercury bougies must be passed by their own weight aided by the peristaltic movements of the esophagus and never by force. Family physicians and even patients themselves can be taught to use these mercury dilators so that the economic advantage over other methods is considerable. Statistically, this method of bouginage will always appear to give superior results since the clinician is unable to determine the actual number of cases which would recover without any or with very little treatment. Experimentally, a standard lesion could be produced in a series of

animals and an accurate assessment made of the value of immediate bouginage compared with delayed bouginage after subsidence of the acute swelling.

After subsidence of the initial swelling, mercury bougies are passed once or twice a week depending upon the amount of swelling resulting from trauma due to the passage of these bougies. This latter swelling subsides in two or three days. Dilatation is always begun each time with a bougie two sizes smaller than the last one used. The largest bougie is allowed to remain in place for 30 minutes.

There is an occasional very severe burn which does not respond to this type of therapy. The stricture progresses so that the retrograde method of Tucker must be relied upon to save the patient.

Vinson passed a blunt olive over a thread to the stricture and thus carefully recorded the exact location of the obstruction in relation to the incisor teeth. Dilating sounds were then passed through the stricture, using a flexible spiral guide over the taut thread. The sounds were passed at intervals over a long period of time. This technique of Vinson's is much like that used by Plummer and Sippy.

Hoag[29, 30] advocated a gradual dilatation of an esophageal stricture by the use of a series of Levine tubes of increasing size and leaving the tubes in constantly. A disadvantage of this method is the development of laryngeal stenosis.

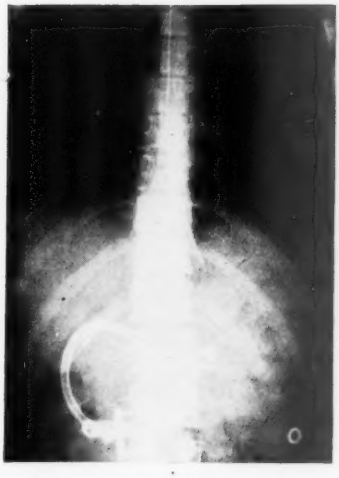
Dean[40] believed electrically heated dilators have a tendency to soften scar tissue thus permitting more effective dilatation.

Abel[6] stated that in long and narrow strictures in which difficulty is experienced in maintaining dilatation, laminaria bougies or tents as used by gynecologists may be placed in position under direct vision and allowed to exert continuous and gradually increasing pressure.

Electrolysis of a stricture may be performed under direct vision by using a current of 15 milliamperes. At the same sitting dilatation may be carried out since electrolysis results in softening of the cicatricial tissue.

Turner[41] believed that each bolus of food swallowed is a valuable dilator.

Conversely, Hoag[29, 30] stated that the impact of food is an important factor in producing and keeping up the secondary inflammation which leads to final closure of the esophagus and that this is



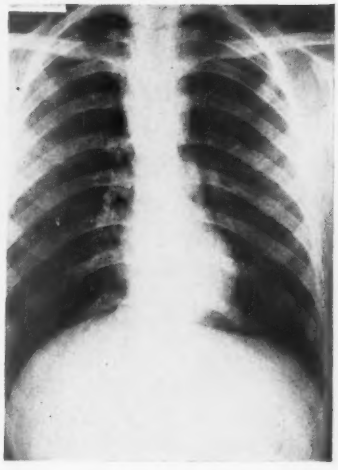


Fig. 1.—Roentgenogram of a lye burn showing complete obstruction at the level of the tracheal bifurcation (See Fig. 2 and the report of a case). The esophogus is dilated at least three times its normal width above the stenosis.

Fig. 2.—Roentgenogram of same case as Fig. 1 two months after gastrostomy, showing sufficient spontaneous reopening of the stricture to allow the passage of a small No. 4 ureteral catheter.

Fig. 3.—Roentgenogram a few hours after an intern made an unsuccessful attempt to pass a Levine tube, showing subcutaneous emphysema in the right side of the neck and mediastinum. The widening of the mediastinum is due to the compensatory dilatation of the esophagus above the stenosis.

evidenced by the fact that when food is administered through a gastrostomy opening as a substitute for feeding by mouth, the esophageal stricture will frequently reopen and again allow food to pass. This latter observation has been observed by all otolaryngologists and reported by many[11, 17, 42, 73] (Figs. 1, 2).

Vinson believed that dilatation from below upwards should not be done because of unnecessary traumatization of the abdominal walls, since all benign strictures should eventually be stretched to size 45 French and introduction of a dilator of that size through a gastrostomy opening is associated with excessive trauma and discomfort.

On the other hand, Tucker stated that patients, especially children, are more tolerant of retrograde than peroral instrumentation and will allow the bougie to remain longer in position when pulled up from below than when brought down through the mouth.

Adams and Hoover[43] are of the opinion that, if a stricture is tortuous or excessive, gastrostomy and retrograde bouginage with Tucker bougies usually is safer than attempting dilatation from above, even with a guiding string.

Billroth noted that the esophagus is bowel-shaped above and funnel-shaped below a stricture, so that a stricture can be entered more easily from below.

Tucker recommended retrograde esophagoscopy and use of the filiform bougies of Jackson to place the continuous string when it cannot be swallowed. Combined retrograde and peroral esophagoscopy under the double plane fluoroscope enabled him to perforate the obliterated part of an esophageal atresia.

Weber[44] in the treatment of a patient with complete stenosis in the lower third of the esophagus and with a gastrostomy wound present for over two years was able by combined peroral and retrograde esophagoscopy under biplane fluoroscopic guidance to force a stiff wire through the atresia. A string was then pulled through and the stricture was dilated to adequate size.

Iglauer,[45] Carroll and Myers[47] and Freiberg[46] described the technique of using a direct-vision cystoscope through a gastrostomy opening in locating the cardiac end of the esophagus and believed that the cystoscope is more easily manipulated than an esophagoscope in combined peroral and retrograde esophagoscopy.

Shaar[75] was successful in dilating a cicatricial stenosis of the esophagus by use of a barium-filled condom attached over a perforation in a stomach tube.

Woodward[64, 65] and Adams and Hoover[7] successfully treated complete strictures of the upper and mid-esophagus by open mediastinotomy, at which time the thoracic surgeon guided the end of the probe inserted by the endoscopist.

Noehren,[48] Yurasov[49] and Fierro[62] described the technique of construction of an artificial esophagus. The mortality rate is high, around 18 to 25 per cent, the procedure is complicated, hospitalization is long and the results are frequently unsatisfactory.

Turner[72] successfully treated a simple stenosis of the cervical esophagus by plastic operation.

Portmann[50] recommended auto-dilatation, that is, the progression of a dilating instrument through the stricture merely under the peristaltic movement of the esophageal walls. An endless silk thread was established coming through the gastrostomy opening below and out of the mouth above. On this thread, Portmann placed three dilating olives of gradually increasing diameter, end to end, with the smallest underneath the other two so that it entered the stricture first from above.

Internal esophagotomy is performed by dividing the stricture inside the esophageal lumen. The mortality rate is around 25 per cent.

An excellent article on corrosive injuries of the esophagus by Truls Leegaard[76] has just appeared in the literature. This author advocated in severe burns external esophagotomy with the introduction of a retained tube.

A gastrostomy is compatible with a long and useful life. Salivary secretions eventually diminish in an atresia so that drooling does not occur. Nevertheless, some surgeons advise spitting of the saliva into a funnel connected with the gastrostomy tube in order to maintain proper nutrition. When a gastrostomy has once been performed, Lower[25] stated that it should not be closed until complete dilatation has been accomplished and maintained for six months to a year.

Complications. Although dehydration and starvation are the most common complications coexistent with esophageal obstruction, many others occur, such as chronic lung infection from regurgitation

and aspiration of food,[66] bleeding, malignant degeneration in the scar of a lye burn, peri-esophagitis with or without involvement of the recurrent laryngeal, vagus and phrenic nerves, mediastinal abscess, ulceration into a large vessel causing fatal hemorrhage, pulmonary gangrene and perforation from ulceration, impaction of a foreign body or instrumentation.

Bleeding usually follows the passage of a bougie or dilating sound during the early weeks of treatment. It may be a warning sign that too large a dilating instrument is being used, although the bleeding is usually from granulation tissue and is not alarming. The bleeding becomes less as the granulation tissue is replaced by fibrous tissue. One danger of bleeding is that the further formation of granulation tissue may be stimulated so that a vicious circle results. Rapid dilatation with force is always dangerous and should never be employed.

According to Vinson the greatest hazard in dilating strictures is that of perforating the wall of the esophagus above the area of scar tissue and he states that such a perforation can be prevented by the use of a guiding thread (Fig. 3).

REPORT OF A CASE

J. W., 149477, white, male, aged 24, swallowed lye in an attempt to commit suicide. He had immediate odynphagia and dysphagia. His dysphagia progressed so that in two weeks he was only able to swallow liquids. One year later (December 8, 1945), on admission to Multnomah Hospital he was unable to swallow even liquids.

One hour after admission an intern made an unsuccessful attempt to pass a Levine tube. Shortly thereafter subcutaneous emphysema appeared in the right supraclavicular fossa. X-ray examination showed air in the soft tissues of the neck, right shoulder and mediastinum. Concomitantly there was a slight elevation in temperature to 99.8° F., an increase in pulse rate to 100 but the respiratory rate remained normal.

The patient was given four grams of sodium sulfadiazine intravenously. An erythematous skin rash appeared. Thereafter he received 15,000 to 20,000 units of penicillin intramuscularly every three hours for 12 days.

Five days after admission x-ray films showed air present as before but much less than on the previous study (Fig. 3).

On the fourth hospital day the temperature and pulse rate became normal.

A gastrostomy was performed. Two weeks later the patient demanded and received a hospital release.

Two months later the patient requested readmission to the hospital. Meanwhile the patient discovered that he was again able to swallow liquids. He was unable to swallow a string. By combined peroral and retrograde esophagoscopy a very small ureteral catheter (No. 4) was passed with difficulty through the stricture from above. A trout fishing line was attached to the catheter below and the string pulled through the stricture out of the mouth. The ends of the line were tied externally near the gastrostomy opening so that a continuous loop resulted. The patient is now undergoing retrograde dilatation with Tucker bougies.

Carmody,[13] Martin,[51] and Imperatori[63] described cases of mediastinitis following instrumentation.

A second type of perforation results during dilatation of the stricture itself and according to Jackson is due to separation of the scar tissue from the normal mucous membrane.

A third type of perforation[71] is that due to spontaneous perforation after prolonged impaction of a bolus of food in the lumen of the esophagus above a stricture followed by forced deglutition.

Adams and Hoover[7] stated that substernal, upper abdominal, or shoulder pain is the most constant sign in mediastinitis. There is a concomitant fever, elevated pulse rate and leukocytosis usually within a few hours of an esophageal procedure. X-ray studies are diagnostic.

The removal of foreign bodies from above, or between, old lye strictures is a common experience with most otolaryngologists[53] (Fig. 4). A recent report[61] indicated that a bolus of meat impacted in an esophageal stricture is completely digested within a few hours by a proteolytic enzyme, papain (caroid). Barium sulfate may completely obstruct a severe esophageal stricture so that in such cases it is advisable to use an opaque iodized oil.

According to Moersch[27] the incidence of impermeable cicatricial stricture, or atresia, in benign cicatricial stricture of the esophagus is about five per cent.

Fig. 4.—Roentgenogram showing a marble above an old lye stricture.

Several authors[54-56] reported incidences of malignant growths developing at the sites of old lye burns of the esophagus.

Since bacillus-laden sputum is being constantly swallowed by patients with active pulmonary disease, it is not surprising that tuberculosis becomes engrafted upon a chemical ulceration or scarring of the esophageal mucosa. Such a case was reported by Myerson.[57]

A logical procedure in the treatment of acute lye burns appears to be the insertion and maintenance of various sized tubes through the esophageal stricture. However, advocates[59, 60] of this treatment found a serious disadvantage in the development of laryngitis, postcricoid abscess and laryngeal stenosis, due probably to pressure of the tubes on the cricopharyngeus and arytenoids resulting in spasm, secondary infection and fibrosis.

Prognosis. The old dictum of Trousseau that "sooner or later all cases of esophageal stricture die of the bougie" is no longer true. Of course, the sooner the patient comes under observation and treatment, the better the prognosis. In the days before common use of the esophagoscope the mortality varied between 40 and 50 per cent. If the patient survives the poisoning and shock of the initial ingestion of the caustic or if the patient develops laryngeal spasm or swelling and has a tracheotomy to prevent suffocation, and then

swallows a string, an excellent functional result can usually be assured.

On the other hand, if treatment is delayed until development of complete closure of the esophagus, inanition and malnutrition may become extreme, normal development considerably retarded and even death may ensue from regurgitation and aspiration of infected mucus.

According to Vinson an average of two years of treatment is required to re-establish and maintain a satisfactory lumen in an esophagus which has been narrowed by scar tissue.

According to Delph[67] a functional cure results in an adult when the lumen of the stricture admits a 7 mm. bougie without difficulty.

Hospitalization. The shortest interval between contamination and initial treatment of any of these patients at the University of Oregon was 15 minutes while the longest period was 60 years, the latter being due to impaction of a foreign body (meat) in an old lye stricture.

SUMMARY

1. The clinical records of all patients treated in the University of Oregon for chemical burns of the esophagus over a 15-year period were reviewed. An analysis of these findings is presented.

2. There were no deaths in this series from peroral instrumentation.

3. The esophageal findings at necropsy of burns due to a silver salt, lactic acid and lye are given. The latter patient with lye burns died with brain abscesses of both temporal lobes, which is very interesting in view of the fact that deaths from brain abscesses under similar conditions have been reported by other authors.

4. The course of action taken at this University in the treatment of acute esophageal burns together with arguments pro and con is discussed.

5. An illustrated case report of an esophagus perforated by a Levine tube used by an intern and of mediastinitis probably prevented by penicillin therapy is described.

6. A patient with a chemical burn of the mouth or pharynx should be considered as having an esophageal burn until it is proven otherwise by esophagoscopy.

The author takes this opportunity to express his appreciation for the critique of this paper and for invaluable assistance on numerous occasions of R. A. Fenton, R. B. Karkeet, Paul Bailey and Bruce Titus.

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LXXIII

THE AURAL REHABILITATION PROGRAM OF THE U. S. ARMY FOR THE DEAF AND HARD OF HEARING*

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Some twenty years before World War II the late Charles H. Mayo made the prophecy that within the next twenty years rehabilitation would prove to be the master word in medicine. When that war began, events were beginning to prove the correctness of his observation. There was a growing realization, frequently translated into action, that while the physician's immediate and urgent task was to save the patient from death and enable him to continue to live, his ultimate responsibility was to see to it that he was restored to complete economic usefulness and to a normal social life, or, if those objectives were impossible, to as close an approximation of normal status as could be achieved. In World War II the Medical Department of the United States Army proved in many fields, of which aural rehabilitation for the deaf and hard of hearing was one, that such an aim was as practical as it was compassionate.

The aurally handicapped soldier was not neglected in World War I. In fact, the school of lip reading which operated for slightly over a year in the Otolaryngological Section of General Hospital No. 11 at Cape May, New Jersey, was described by Berry[1] as "one of the bright spots in the Army's reconstruction activities." But its usefulness, unfortunately, was limited. In all, it served only 108 war-deaf soldiers, although in October 1943 the Veterans Administration had on its compensation or pension rolls 416 totally deaf veterans of that war and 12,397 partially deaf.[2] The exact figures are not available, but there seems little doubt that in World War I, just as in World War II, a very large proportion of these veterans suffered from some form of aural disability before their induction into service.

In World War II the importance of the problem of the deaf and hard of hearing soldier was grasped at an earlier period than in

*Unless otherwise specified, the material in this account is derived from the histories of the Army Aural Rehabilitation Centers for the Deaf and Hard of Hearing at Borden General Hospital, Deshon General Hospital, and Hoff General Hospital.

World War I and at this writing, more than a year after the close of the fighting in Europe and almost a year since the close of the fighting in the Pacific, one of the centers (Borden) is still operating. In May 1943 specialized centers for the treatment of these casualties were designated at Borden General Hospital, Chickasha, Oklahoma, Hoff General Hospital, Santa Barbara, California, and Walter Reed General Hospital, Washington, D. C., the latter center being transferred some six months later to the Deshon General Hospital, Butler, Pennsylvania. In all, approximately 8,400 deaf and hard of hearing soldiers were treated in the three centers during their approximately three years of operation.

HISTORY AND PLAN

By this time the history and the operational plan of the Army aural rehabilitation program are probably well known. The original program was a function of the Reconditioning Division of the Surgeon General's Office, and while all three centers were under a central organization, for all practical purposes they operated as individual units. In February 1944 the late Dr. Walter Hughson,[3] reporting on a visit to one of the centers and a survey of the program which he had made at the request of Brigadier General Fred W. Rankin, Chief of Surgical Consultants, deplored this situation. As a scientific otologist, he stated, he regarded the implications of a program involving a large and completely controlled number of cases as of the greatest significance for the present and future of civilian as well as of military otology, but if the program were to have this value, a completely unified method of examination and recording was essential in all three centers. He also pointed out the need for the administration of objective tests by qualified personnel to determine the instructional needs, potentialities and progress of each patient, on the ground that a satisfactory remedial program could not possibly be planned for any casualty without first measuring his mental ability, educational background and general language status.

In June 1944 Brigadier General Rankin,[4] following a visit of inspection to two of the three centers, reported to the Surgeon General that although the deaf and hard of hearing casualties had to date received excellent care, he regarded it as essential for future progress (1) that the activities of all three centers be made uniform, (2) that equipment be standardized, and (3) that a standard policy be adopted for the procurement of hearing aids, with complete exclusion of all commercial contacts. To carry out these recom-

mendations General Rankin recommended that an otologist be placed on duty in the Surgeon General's Office, who would devote his full time to the deaf program. In July 1944 the writer, who formerly had been Chief of the Eye, Ear, Nose and Throat Service at Borden General Hospital, and in charge of the center for the deaf and hard of hearing at that installation, was placed on duty in the Surgeon General's Office as Chief of the newly organized Otolaryngology Branch in the Surgical Consultants Division, and shortly afterward the plan of organization which he had recommended to General Rankin was put into effect at all three centers (Fig. 1).

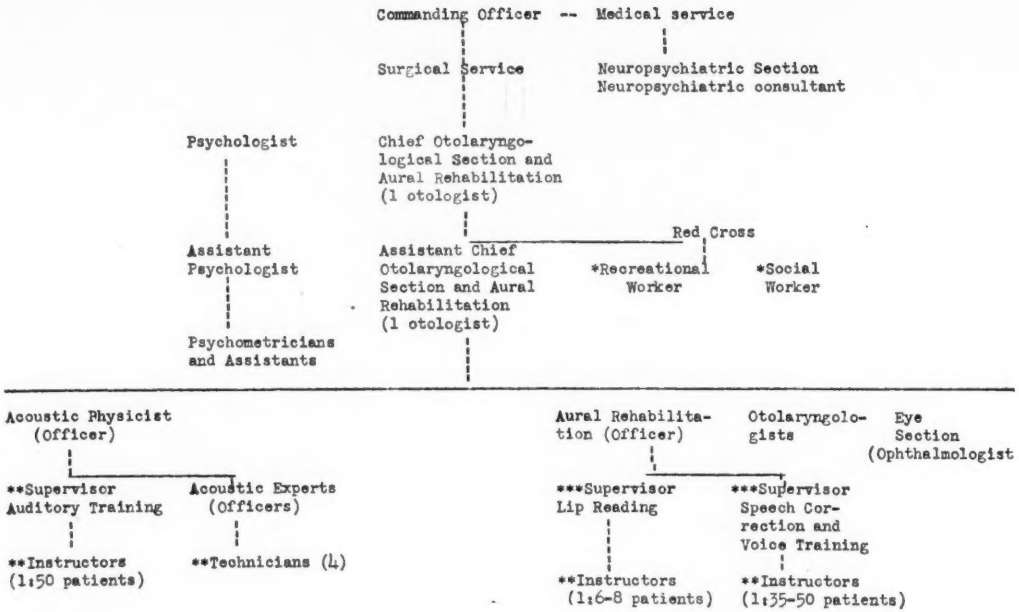
By this organization, it will be noted, an otologist was in charge of the entire program. His medical assistants were responsible, under him, for diagnostic and therapeutic supervision of the patients, and those in charge of various levels of non-medical instruction and other non-medical activities supervised, under higher direction, the personnel and programs on their respective levels. It should also be emphasized that although compliance with the basic organization was insisted upon, the program was sufficiently elastic to encourage individual initiative; the projects carried out at each center make that clear. By virtue of the central organization, however, and by means of the bimonthly reports from each center received in the Otolaryngology Branch in the Surgeon General's Office, it was possible to exchange suggestions and plans, as well as to evaluate them. The visits of the Chief of the Otolaryngology Branch to the various centers also made possible the rapid utilization in all centers of plans and procedures which had proved of value in one center.

In substance, the routine of rehabilitation was eventually standardized at the three centers about as follows:

1. The patient was admitted to one of the medical wards reserved for this purpose, on which:

A. A complete history was taken and a complete physical examination was made by the ward officer, and routine laboratory studies (urinalysis, blood count and serologic tests) were carried out. Roentgenologic examination of the mastoid region was made in all cases and other examinations, particularly of the chest, were made on special indications.

B. Consultations were requested as necessary with the surgical, neuropsychiatric, dental and other sections. Ophthalmologic examination was part of the initial routine.



*Full time. **Enlisted or civilian ***Commissioned officer or civilian.

Fig. 1.—Organizational structure at specialized center for the treatment of the deaf and hard of hearing.

C. A complete otolaryngologic study was made, including: a detailed history and physical examination; tests of vestibular function; determination of the patency of the eustachian tubes; tests of hearing, including fork tests and complete air conduction and bone conduction audiometry; other special tests as necessary.

Audiometric testing was carried out at all three centers by a strictly prescribed routine, the instructions to the examiner covering the following points: preliminary questioning of the patient and specific instructions to him concerning his part in the testing; the seating of the patient in relation to the testing instrument; the environment, which was always a sound-treated room; the attachment and method of operation of the audiometer, which varied with the type of instrument employed; the careful recording of results.

D. Upon the conclusion of these studies, a diagnosis was made of the etiology and type of hearing loss. If the patient's disability did not fall within the prescribed limits, he was dismissed from the center. If it did, he was referred to the Rehabilitation Officer and admitted to the rehabilitation course.

2. Initial testing in the rehabilitation course consisted of:

A. Repetition of air conduction and bone conduction audiometric testing.

B. Tests of auricular ability, including monaural distance ratios for spoken and whispered voice recognition; binaural percentages of phonetic discrimination; and binaural distance thresholds for perception of connected speech.

C. Tests of visual identification of word and sentence meanings were made to determine lip-reading ability.

D. Systematic speech sound articulation inventory and voice check was made.

E. Psychologic testing, including intelligence, special aptitudes and personal composition was done.

F. A social case history was taken.

3. Upon completion of these procedures, patients not actually in need of hospital care for aural or other reasons were transferred to the convalescent unit and were assigned such duties as would be performed by any other ambulatory patient, kitchen police being no exception. Physical exercise, under supervision, occupied at least an hour daily, and provision was made for both indoor and outdoor

recreation. Daily, weekend, and extended (three-day monthly) passes were encouraged, ordinary social contacts being regarded as the best possible method of having the soldier put into practice the abilities in which he was being trained.

4. The rehabilitation program included the following courses:

A. Lip Reading. This course included training in sounds, words, sentences, conversation, lectures and moving pictures. The material, which was largely original, was adapted to the educational background, occupation and interests of the special patients. Much of it, indeed, was eventually contributed by the patients themselves. At the Hoff Center two books of original lip-reading material were developed, "A Framework of Instruction in Lip Reading," and "Tales of Hoffmen," both of which contain practice material largely based upon individual experiences. Methods of instruction were elastic and included both individual and group teaching. The instruction at each center stressed the importance of taking advantage not only of the movement of the speaker's lips but also of his facial expression and other visual clues to the purport of what was being said.

B. Auditory Training. This course was begun as soon as possible after the patient's admission, even before a hearing aid could be secured. It included individual and group conversations against a silent background and a background of various noises. From conversations the students progressed to lectures, music, radio, moving pictures, telephone conversations and natural sounds. Material was presented at gradually increasing distances. Whatever the method employed, the objective of the course was the same, to train the patient to listen attentively and so to employ his residual hearing and the hearing available to him through his hearing aid as fully as possible.

C. Voice Training and Speech Correction. The need of the individual for this instruction was based on observation of his individual defects as determined by words, conversation and reading selections, the test being related to his previously determined intellectual abilities. The course included instruction in ear training; tongue, lip and jaw gymnastics; breath control; sound analysis with relation to special defects; and drills on corrected speech habits. Attention was paid to pitch, timing, and loudness and quality of the voice, as well as to articulation.

D. Speech Insurance. This course was given to men with severe hearing losses to guard against future speech deterioration. In

general, it was designed for patients in whom deterioration, in the absence of prophylaxis against it, might be expected to occur, though it was sometimes found desirable in individual cases to give the course in combination with speech correction. As in the latter course, attention was paid to pitch, quality and loudness of the voice, as well as to articulation, though the teaching approach was naturally different.

Space does not permit the discussion of many other phases of the Aural Rehabilitation Program, including the social and family services supplied by the Red Cross; the contacts established with the Veterans Administration; the opportunities for recreation, occupational therapy, and training in such occupations as auto mechanics, watch repairing, creamery management, cleaning and pressing, and similar useful occupations. The driver training course conducted by the Hoff Center in the sixth week of the rehabilitation course was particularly successful; at the conclusion of instruction tests were conducted and licenses given by the California State Department of Motor Vehicles. Every patient, in short, was provided with all possible opportunities to keep himself occupied, and while recreation was encouraged, emphasis was also placed, directly and indirectly, upon useful occupation with the realization that the "disintegrating effects" of idleness are perhaps the most serious obstacle which any disabled man must overcome.

Hearing Aids. The chaotic situation which had originally existed in respect to the fitting and procurement of hearing aids was altered in two ways in the reorganized program, by the development of scientific tests to determine the special aid suited to the needs of the individual patient, and by the complete separation of the patient from any contact with representatives of the manufacturers of the aids. All aids employed in testing were on the recommended list of the Council on Physical Medicine of the American Medical Association. After November 1944 the lucite ear tip for the aid was made in the dental laboratories of the hospitals at which the centers were located, with great savings in time and money. Still later, indefinite quantity contracts were closed for the purchase of the aids found on survey to be most frequently used, great savings being effected by this plan in view of the numbers required; the original plan of purchasing aids locally as they were needed had always been recognized as uneconomical, but until adequate data were at hand it was also recognized as a necessity. Under the new plan it was still possible to purchase aids not covered by the contract if they were found more suitable for special patients. Testing of new models put out

by all manufacturers was continued, regardless of the contract status of the company, so that the savings effected by the contracts in no wise militated against the continued initiative of any commercial concern.

In general, an air conduction receiver was always fitted unless the patient had a chronic suppurative process or unless bone conduction, as measured by the audiometer, was good and air conduction testing indicated poor correction with an air conduction receiver.

If the patient presented an approximately equal, uniform, bilateral, moderate loss, the ear not used for telephone conversations was fitted. If the poorer ear had less than (approximately) 70 decibels loss in the speech range, the poorer ear was fitted; otherwise the better ear was fitted.

The Acoustic Officer or a qualified assistant, following study of the audiogram and other special tests, plotted six or seven possible fittings for each patient. Each fitting was arranged in turn on the patient who, following careful previous instructions, adjusted the volume while selected sentences were read to him at constant distances. At the Deshon Center a speech discrimination test was conducted in advance of the fitting of the aid and a screening period preceded the regular fittings. The technician tried a number of aids, in various combinations of models, and ran brief preliminary tests to determine which instruments and which combinations were suitable for further testing. Binaural free field audiometric testing was carried out at the Hoff and Borden Centers.

At all three centers careful tests were conducted to determine speech articulation thresholds. These tests were followed by determination of the tolerance threshold and the preference level. As a final step, the aid was turned on in full volume to determine the reserve amplification possible with the instrument. The patient was encouraged to express his opinion as to clarity, naturalness, quietness of reception, and other features of the instrument being tested, but leading questions were avoided and except at the Deshon Center he was kept unaware of his own share in the selection of the aid. At that center the patient wore each instrument under consideration for final selection for a 24-hour period and also at a listening hour, and indicated on a scale its performance for speech, music and noises.

The patient was carefully instructed as to the method of using the instrument finally selected on the basis of the recorded results of all tests. At first it was necessary to remind him constantly of the

necessity of adjusting the volume and tone control according to the circumstances of listening; later these adjustments became automatic. At the end of a week, if the instrument did not prove satisfactory, additional instruments were tested. During the period of testing the patient reported regularly to the acoustic technician or to a designated teacher of auditory training for necessary adjustments. When he received the instrument, he was given printed instructions concerning its care, and in the first weeks of its use he received further individual and group instruction concerning its proper care, including daily rotation of the batteries and methods of securing the fullest possible aid from it. When he left the center he was given a month's supply of batteries.

Narcosynthesis. One of the outstanding developments of the Aural Rehabiliation Program was the management of cases of psychogenic deafness, which in some instances was also associated with true organic damage. Narcosynthesis was tried in these cases because of the excellent results of the method reported by Colonel Roy R. Grinker during the North African campaign. Cases were selected most carefully and treatment was carried out under the joint direction of the otologist, the psychiatrist and the psychologist. Individual and group suggestion was practised before narcosis with sodium pentothal was undertaken. Narcosis was light and very carefully controlled. During the period of narcosis the patient was asked simple questions and was repeatedly assured that he would recover his hearing. The assurances were continued for an hour or two after narcosis was discontinued. Audiometric and spoken and whispered voice tests were recorded as soon as possible after treatment, the tests being carried out by a technician who had been specially trained for the work by a psychologist, and were repeated as often as necessary on successive days to determine the threshold of hearing. Recorded speech perception tests were run if there were any question as to the results of the live voice tests. Psychologic evaluation was an important part of the cure. It has been estimated that some 15 per cent of the cases of deafness treated in the Army centers were of the hysterical or psychogenic variety, the group including numerous cases in which the disability was of long standing. The results of narcosynthesis were remarkably good; 74 of the 80 cases of hearing improvement observed at the Hoff Center between February and October 1945 had been treated by this method.

Individualization of the Routine. The routine described was placed in effect, within an elastic framework, at each of the aural rehabilitation centers, but it was carefully individualized in every

case. When data secured in the various preliminary tests had been recorded on appropriate forms, they were reviewed by the Aural Rehabilitation Officer who had a personal interview with the patient, and were discussed by a consultation board which met weekly and which, on the basis of its discussions, outlined an individual course of study for each patient. The board, in addition to the Aural Rehabilitation Officer, consisted of the Director of Rehabilitation, the ward officers, and the supervisor of each department.

The preliminary evaluation was essential because the wide variation in intelligence and in the intellectual and educational backgrounds of the patients made individualization of his rehabilitation extremely important. A study of a sample at the Hoff Center, for instance, makes this point clear: The age range was from 18 to 58 years, two-thirds of the patients being between 22 and 32 years. Seven and two-tenths per cent were college graduates, but 0.8 per cent were illiterate and were taught to read and write as part of their rehabilitation. Eight and six-tenths per cent were commissioned and 31.6 per cent non-commissioned officers. Fifty-three and two-tenths per cent had previously followed unskilled occupations, but 5.4 per cent were professional men. The hearing disability had been present only a few months in 15 per cent, less than four years in 33 per cent, over four years in 63 per cent, and over twelve years in 31 per cent.

During the eighth week of the rehabilitation program, or sooner if the patient's level of achievement warranted it, the Aural Rehabilitation Officer again interviewed the patient and personally evaluated his progress. The Director of the Program, after he had studied the record, then interviewed the patient and made his own evaluation to determine the need for further hospitalization for medical or other reasons, for further participation in the rehabilitation program, or for processing for disposition according to the Army directives effective at the particular time.

Students in the lip-reading course were graded as excellent (capable of making an intelligent response to any situation requiring the understanding of speech); good or above average (showing a high degree of mastery of every day speech); average (possessing a working ability to understand speech with occasional repetitions in ordinary circumstances); and below average (possessing some knowledge of lip reading, which might or might not be useful). There was often a curious difference between the instructors' evaluation of the students' ability and the students' estimate of their own prog-

ress. At the Hoff Center, in one survey, a third of the patients were rated by the instructors as excellent, about two-fifths as good or average, and the remainder as below average, but at the same time only one per cent of the students graded themselves as excellent and only ten per cent as above average. Sixty-four per cent, however, believed the course to be of great value.

Individual analysis of the patient's needs materially reduced the number given speech training. In one survey at Deshon General Hospital it was found that while 30 per cent of the students had evident speech abnormalities, many of them were of the social and economic strata in which such abnormalities could be disregarded. In other instances the abnormalities were purely dialectical. In all, not more than ten per cent of all patients presented speech abnormalities which could be related to their hearing impairment and which therefore were in need of correction.

PRACTICAL CONSIDERATIONS OF THE AURAL REHABILITATION PROGRAM

It should be emphasized that the problem with which the Army found itself confronted in the rehabilitation of the deaf and hard of hearing soldier had no precise parallel in civilian life, either in its magnitude or, in some instances, in the circumstances under which the loss of hearing developed. Surprisingly, however, the number of abruptly deafened soldiers, whether from blast or from head injuries, was considerably smaller than had been anticipated, while the large numbers of casualties expected from the Air Force simply did not materialize. Studies of blast injuries suggest that about two-thirds of the men thus injured suffered no permanent impairment of hearing, while only a small minority of the remaining third suffered sufficient hearing loss in both ears to require rehabilitation and a hearing aid. About 60 per cent of the cases of psychogenic deafness, however, were of combat origin. It is of interest that while meningitis accounted for about 25 per cent of the deaf casualties of World War I, the number from this cause in World War II was negligible, undoubtedly because of the remarkable effectiveness of chemotherapy in control of the disease.

There was, of course, nothing in common between the rehabilitative problems of the deaf soldier and the problems presented by civilians who were either born deaf or who had lost their hearing before they learned to speak. The deaf or hard of hearing soldier, whether he lost his hearing suddenly or his previously impaired hear-

ing was still further impaired during his military service, suffered his disability after language patterns were established. Material to teach adults who presented such disparity of social, intellectual and educational backgrounds for the most part did not exist, and its improvisation was one of the chief tasks of the early days of the program.

In addition to the lack of suitable teaching material, two other special difficulties made themselves evident at the institution of the program. The first was that trained personnel was completely lacking for speech instruction and auditory training, as well as personnel trained in acoustic physics to build, install and maintain the electroacoustic equipment essential in the program. This difficulty was overcome in a variety of ways. All organizations working in the field were solicited for names of qualified personnel. The Adjutant General's files were reviewed to identify Army personnel with specialized training. Qualifications of WACs in service were studied, and a WAC recruitment program was instituted for training for this special purpose. The New Developments Branch of the War Department and the National Roster of the War Manpower Commission were also investigated. Advertisements were placed in appropriate magazines to attract teachers through civil service. Finally, a procurement objective for acoustic and rehabilitation officers for the deaf was authorized by The Adjutant General in June 1944.

The retention and proper assignment of the specialized personnel proved no simple matter. It was found on early visits to medical installations that otologists specially trained for the Aural Rehabilitation Program were sometimes being assigned to other duties, in which their specialized skills were not fully untilized or were not utilized at all. The importance of retaining intact the organization which had been set up was explained to all Service Commands, and the time, effort and expense expended in the training of these officers was emphasized. Eventually, in February 1945, a War Department memorandum[5] directed attention to the importance of retaining critically needed specialists in their special capacities and listed among such specialized personnel psychiatric social workers, specialists in teaching lip reading, speech correctionists and acoustic technicians.

The other great difficulty of the early Aural Rehabilitation Program was concerned with procurement of the highly specialized equipment needed. For a long time this was the most serious bottleneck in the whole program. Specially constructed acoustic buildings with calibrated, soundproof rooms were required to house the

electro-acoustic apparatus used in the measurement of hearing, and it was not until the fall of 1944 that the major portion necessary was secured and installed in the three centers. Part of the delay was due to shortages of materials, part to limitations of manufacture, and part to the needs and claims of other agencies, chiefly the Signal Corps, Ordnance, and the Office of War Information. In July 1944 all three centers were still without such basic items as sound level meters and magnetic tape recorders, but by November of that year most of the essential equipment had been installed in all centers and was in operation under a standard, uniform plan directed from the Surgeon General's office.

At the beginning of the program the stipulation that military personnel with "defective hearing of a degree which precludes the return of the patient to duty" was interpreted as a hearing loss of 60 decibels, which, as the late Dr. Hughson[3] pointed out in his report to General Rankin, was "entirely improper and unjust." At the January 1944 meeting of the Subcommittee on Otolaryngology of the Division of Medical Sciences of the National Research Council it was recommended that, "Cases showing an average loss of 30 decibels in the better ear for the frequency of 256, 512, 1024, and 2048 be considered in need of a survey at one of the Army special centers, provided that they have no remedial defects." Thereafter deaf and hard of hearing casualties were referred to the special centers on this basis.[6]

Originally the prescribing and fitting of hearing aids at the three centers was limited to men whose hearing impairment had been suffered in line of duty, which of course excluded the large number who had been inducted into the Army with existing impairment of hearing. The distinction naturally resulted in considerable feeling on the part of the Line-of-Duty-No men, who were frequently aware that the methods of screening used in induction centers were crude and who resented the fact that they were not given aids, particularly if their impairment had been increased (or if they believed that it had been increased) by service. In February 1944 this policy was altered and aids were furnished to all deaf and hard of hearing men in service, regardless of when or how the impairment had originated.[7]

How many men were inducted into service in World War II with existing hearing defects it is not possible to say, but there is no doubt that the number was large. Prior to March 15, 1942[8] acuity of at least 15/20 in one ear and 20/20 in the other was

required for enlisted men, applicants for commissions in the National Guard, and service in the organized reserves, while hearing of 20/20 in each ear was required for a commission in the Regular Army. Limited service in some categories was provided for if the hearing did not meet these criteria. These requirements were modified, as the war progressed and the need for manpower became more acute, until the Regulations of April 19, 1944,[9] which provided for hearing of 8/15 or better in each ear, or of 15/15 in one ear and less than 8/15 in the other. In these Regulations the testing distance was first reduced from 20 to 15 feet and the whispered voice test was substituted for the low conversational voice test.

In addition to the progressive lowering of standards of hearing, it is well known that the tests employed were not accurate in themselves and that the circumstances under which they had to be given, in crowded and noisy induction centers, further militated against their accuracy. It is not surprising that in the neighborhood of 40 per cent of the men treated in the aural rehabilitation centers were classified as EPTI (meaning that the disability had existed prior to induction) or that in many such cases the induction record bore the notation that hearing was normal.

In all three centers it proved almost impossible to keep the patient load and the provision of facilities on the same level. At the Deshon Center, for instance, the initial calculations were for a patient load of 250, but the load was 400 before facilities for the initial load were provided. By the time the facilities had been brought up to the 400-patient level, the population of the center numbered 500. When the census reached its peak at this center, August 12, 1945, it was necessary to schedule classes at night as well as during the day. The patients did not suffer, except for some loss of the intimate and personal contact of physician and patient which is part of the art of medicine. Had the load been sustained, however, as it would have been had hostilities continued, a break in operational efficiency would undoubtedly have occurred, which would have prolonged the hospital stay of the individual patient or would have caused the creation of a backlog of the many patients sent out on furlough status.

A very wholesome aspect of the Army's Aural Rehabilitation Program was its perfectly realistic approach to the whole problem of loss of hearing. There was complete realization, as Hughson[3] expressed it, that the "psychologic implications" of deafness are probably "more important than any which will develop as the result

of a physical disability," as well as complete realization that in many instances it would be difficult, if not impossible, to disentangle the psychologic threads, so to speak, and to separate the trauma imposed by deafness from the mental and spiritual trauma inherent in the sights and sounds of combat. On the other hand, the utmost care was taken to see that a deaf casualty who was not a psychiatric problem when he entered the center did not become one.

A special effort was always made to make clear to each patient precisely what he could expect from the rehabilitation course. It was explained unequivocally that a completely deaf or a seriously deaf person could not expect to regain his full hearing but that he could be taught methods of compensating for his disability. It was emphasized that nothing could be accomplished without his own full cooperation and it was only in the exceptional case that such cooperation was not given. In fact, the psychologists and psychiatrists who participated in the program often commented on the lack of resentment expressed by these patients in respect to their handicap, in contrast to the resentment frequently felt under the same circumstances, and on their excellent adjustment. Those in charge of the program were quite convinced that this attitude on the part of the patients was in large part the result of the realistic attitude of the staffs of the centers, which was that in serious auditory impairments lip reading, hearing aids, and other measures even at the best compensate only partially, and that social, vocational and economic readjustments may be necessary to solve the problems of any individual patient.

Another reason for the normal and well-adjusted attitude of most of the deaf and hard of hearing patients was their prompt removal from the hospital atmosphere. The great majority required no otolaryngologic treatment. A few presented sufficient lymphoid tissue in or about the orifice of the eustachian tubes, with enough tubal and middle ear disease, to warrant transfer to a radiation center for treatment, and an occasional sinus operation and tonsillectomy, and a still more occasional mastoidectomy, were performed. But most of the patients were not ill and when their preliminary testing was completed, they were promptly transferred to convalescent units, where they lived as normal lives as can be lived by men still under military control. At the Hoff Center the circumstances were particularly propitious, for the patients were housed in a well-converted public school building, several hundred feet above the Pacific Ocean, in a stimulating and beautiful environment. Although at the Borden and Deshon Centers the barracks used for the convalescent units were temporary buildings equipped with Army bunks, few of the antici-

pated complaints as to the discomfort of the arrangements were heard. The men apparently appreciated the social contacts, liberal passes and other privileges which could not have been permitted under the regimentation and discipline essential in hospital wards, and the contact, in turn, proved an important phase of their rehabilitation.

A particular attempt was made to explain to the patients that hearing aids, at least in their present state of development, have a limited usefulness. The tendency of the lay public to compare them with glasses, usually to their detriment, is unfortunate; a lens corrects an error in refraction, while the best of hearing aids merely amplifies sounds. It was fully realized by the staff that the fitting of the aids, in spite of every endeavor to select them objectively, was still largely a trial-and-error performance. In this connection, it is of interest that Davis and his co-workers[10] at the Psycho-Acoustic and Electro-Acoustic Laboratories of Harvard University have recently expressed the opinion, as the result of exhaustive studies, that present objective tests for the fitting of hearing aids are too arbitrary, too elaborate or too inconclusive to be made the basis of a general routine procedure. Their criticisms are at least disinterested, since several of them themselves helped to develop some of the tests depreciated. Nor can there be any quarrel with the future objectives they have set: (1) That objective tests be simplified and designed to insure accuracy in essentials rather than to try to discover a uniqueness of fit which rarely if ever exists. (2) That both tests and routine be designed to identify any special problem or unusual feature of the individual case which may require special or unusual procedures. (3) That the medical and psychologic aspects of the problem, including the indoctrination and training of the patient, be kept in mind at all times.

Unfortunately, no adequate follow-up studies were possible on these patients, who became the responsibility of the Veterans Administration when they were discharged from the Army. The Deshon Center in a 300-reply response to 500 questionnaires sent out found that 94 per cent of those who responded were satisfied or very well satisfied with the performance of their hearing aids. The personal impression of workers in the program is that a large proportion of the patients returned to civil life have made highly satisfactory adjustments, and numerous individual instances are known, particularly among those whose hearing was impaired before their induction into military service, of higher standards of living than had previously existed. Walter,[11] reporting on the program

for the vocational rehabilitation of the deaf and hard of hearing in Pennsylvania, recently stated that over a period of years 85 per cent of the disabled persons followed up were working for the same employers as the year before, about the same percentage were working in the employment for which they had been trained, 40 to 50 per cent had had wage increases, and the group as a whole was efficient and stable. Whether the results would be as good in the Army program is doubtful. The country naturally must be responsible for the men disabled in its service, but one need not be a cynic to point out that a regular pension is sometimes a deterrent to regular employment.

SUMMARY AND CONCLUSIONS

Although there is nothing new about the problems of patients who are deaf and hard of hearing, the number of such impairments observed in the United States Army and the responsibility assumed by the Medical Department for them, permitted a study of the whole field of deafness never possible in civilian life. Much of the accumulated data, analysis of which is now under way, confirmed previous impressions, many of which can now be regarded as facts. Many of the data are inconclusive, though they point the way to further fields of study.

The integration of the program is perhaps its most significant aspect. For the first time there were put under a single roof, in largescale collaboration, all of those concerned with the problem of the deaf and hard of hearing patient, including the otolaryngologist specially trained in otology, the acoustic engineer, the teacher of lip reading, the teacher of auditory training, the speech correctionist, and the social worker. Every member of the staff was a specialist in his own field. Some teachers were themselves as handicapped as their pupils and were vital and inspiring illustrations of how handicaps can be overcome. Each center was provided with the best and most modern equipment. Every phase of the program was carefully planned, with the object of making it as intensive and at the same time as streamlined as possible.

Although the Army Program of Aural Rehabilitation was evolved for military purposes, there seems no reason why it should not be applied to the problem of civilian deafness. Indeed, it would be a great wastage of effort if the knowledge and experience were not transferred. A program which involves the integration of trained personnel, clinics, laboratories, electro-acoustic equipment

and classrooms under a single roof would seem an ideal set-up for a community attack upon a local problem. It should be emphasized, however, that in the institution of such a program two principles are fundamental, that auditory impairment is primarily a medical problem and that an otologist must always be in over-all charge of the plan.

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LXXIV

A STATISTICAL ANALYSIS OF AUDIOMETRIC SURVEYS IN THE ROYAL CANADIAN AIR FORCE

HONORARY WING COMMANDER JOSEPH A. SULLIVAN, M.B., AND ASSOCIATES

ROYAL CANADIAN AIR FORCE

The purpose of this presentation is to add emphasis if possible to the need of correcting existing deficiencies in evaluating hearing ability encountered both in the First World War and the just recently ended world conflict. Up to the present time the work done by the Royal Canadian Air Force Otological Laboratory Group at the University of Toronto has been to a great extent of a general nature. While the ultimate aim of the organization has been the development of apparatus that would be of aid in the diagnosis of various ear diseases and the development of a practical hearing test for the selection of personnel, much ground work has been done on sidelines, such as hearing surveys and consultation cases. These, while not contributing directly to the main problem, threw some light on what was to be required in a good hearing test and the practical difficulties which would be encountered in the operation of such a test.

It is to the physicist and the acoustical engineer that the otologist must turn for clarification of the basic nature of sound. While the whole field is important and vital, for the physician it is most important that he know the derivation of basic sound measurements and also what means exist to measure sound.

Sound energy can be expressed as microwatts, dynes per square centimetre or more commonly in decibels. There are definite mathematical formulas which express these relationships accurately.

A working definition of the decibel would be that it is the smallest unit of sound perceived. Between the threshold of feeling and the threshold of pain for a sound of a definite cycle, there is a range of about 130 decibels. Most human beings can perceive sound

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of the nature of 20 to 20,000 cycles per second. But only the frequencies up to 2048 make up the usual speech range with the bulk of the intelligible range in the neighborhood of 1000 cycles per second. The basic decibel unit as used in this country has been obtained by actual measurement of groups of normal persons in their response to a tone of 1000 cycles per second. So that when an industrial noise or any other noise is said to have a value of 50 decibels, it should be understood that it is being compared with an intensity of a tone of 1000 cycles. Such a measurement has obvious disadvantages, but it has provided otologists with their only means of measuring and standardizing noise levels so that different studies can be correlated and definite thresholds set.

For the physician, particularly the otologist, we have been at a complete loss, up to the present time, in being able to carry out a hearing test so that the technique of such a test is the same wherever performed. The application of a pure tone audiometric test, the live voice test and the recorded speech test have all been undertaken. For measuring hearing loss, we have used Maico audiometers and have calibrated them frequently enough to give us a knowledge of their behaviour. The calibration technique was devised by the United States Bureau of Standards and the Cruft Laboratory at Harvard University.

The calibration of an air conduction receiver of an audiometer is a matter requiring great precision in measurement. The standard to which the calibration measurements are referred is the results of the National Health Survey Hearing Study of 1936. At the United States National Bureau of Standards, Washington, D. C. there are three standard receivers; Western Electric type 705 A, for which the voltages required to produce the standard average threshold level in the average ear as determined in the 1936 survey are known. To calibrate an unknown type of receiver a loudness balance test is made between the unknown receiver and the three standards in turn on at least ten to twelve subjects. This is effected by listening to the unknown receiver with one ear and then listening to the standard receiver with the same ear and so on, the voltage of the unknown receiver being adjustable to facilitate balance. By measurement, the magnitude of the voltage required to produce loudness balance between the two receivers is obtained. In order to minimize errors in balancing, the same test is performed at three intensities, namely, threshold, 20 decibels above threshold and finally 40 decibels above threshold. The average voltage obtained in the tests is taken as a standard of that particular type of test receiver. By use of a cali-

brated Western Electric type 640 AA condenser microphone and a special type of coupler for use with air conduction receivers, developed by the Bureau of Standards and designated by the prefix number 9, the pressure developed in the cavity of the coupler by the test receiver can be measured.

Because of the difficulty of measuring such pressures in the region of threshold pressures it has been found satisfactory to make such pressure measurements for an applied voltage of plus 60 decibels above the threshold voltages as determined by the loudness balance standardizing test just described. From these measurements the pressures developed under these conditions can be taken as a standard for this particular type of receiver.

In the case of commercially produced audiometers the pressures produced in a No. 9 coupler have been determined for each type of air conduction receiver used by the audiometer manufacturers. It is from the results of these measurements that our audiometers can be calibrated under laboratory conditions similar to those of the standard laboratory. The actual apparatus used in our laboratory to perform this calibration test is shown in Fig. 1. This consists of a wave analyzer and a sound pressure meter; the latter is an instrument developed by the Cruft Laboratories, and consists of a Western Electric type 640 AA condenser microphone and an impedance matching circuit. In order to couple the test receivers to the pressure meter a brass replica of the Bureau of Standards No. 9 coupler is employed. A second device makes certain the test re-

TABLE 1.

WESTERN ELECTRIC RECEIVER, TYPE 711, SERIAL 11.

FREQUENCY IN CYCLES PER SECOND	BUREAU OF STANDARDS RESPONSE IN DECIBELS RE 1 DYNE PER SQ. CM. PER VOLT	UNIVERSITY OF TORONTO RESPONSE IN SAME UNITS AS PREVIOUS COLUMN
256	49.6	49.5
512	48.3	48.1
1024	43.7	44.5
2048	42.3	39.9
4096	43.6	43.1
8192	37.4	39.3

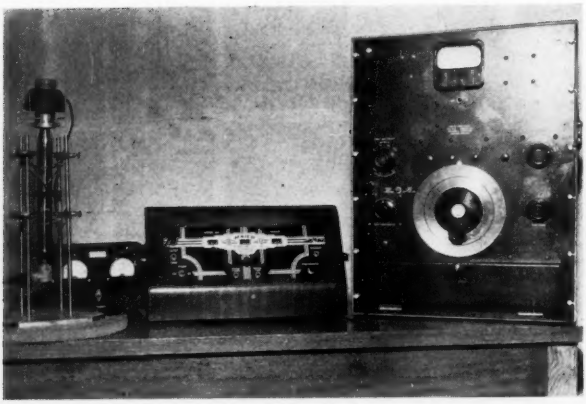

Fig. 1.—Arrangement of apparatus for calibration of audiometers.

Fig. 2.—Mobile soundproof room.

ceiver remains in place on the knife edge of the coupler during the calibration. To ensure a good seal between the coupler and the test receiver the rubber cushion of the receiver is left in place and an additional weight of approximately 400 grams is added to the receiver's weight. From the result of standardizing tests carried out at six-month intervals on the pressure meter and the brass coupler by use of a standard Western Electric type 711 air conduction receiver loaned to us by the Bureau of Standards, it is possible to use such a device as an accurate measuring instrument. It might be noted here that it has been found by the Bureau of Standards that a high quality receiver will retain its calibration indefinitely compared with that of the pressure meter (Table 1).

By conversion of the pressure, generated in the cavity of the coupler by the condenser microphone, to electrical energy it is possible by means of the wave analyzer (an instrument capable of measuring the magnitude of the fundamental frequency component of a wave and rejecting all other harmonics present) to determine the actual magnitude of the pressure developed in the cavity of the coupler by the test receiver. On comparing these pressures with the standard pressures for that particular type of receiver under similar conditions it is possible to determine the magnitude of error of the test receiver with an exact degree of precision.

For our field surveys a mobile soundproof room was constructed. The room consists of three cylinders of 3/16 inch steel. The outer cylinder has an anteroom attached to it. The internal diameter of the innermost cylinder is 6½ feet; the height of the innermost cylinder is about 7 feet. Doors are 5 feet by 22 inches. A porthole 14 inches in diameter permits vision from the anteroom through the two inner cylinders. Artificial light is necessary and is taken from an adjacent building. Ventilation depends on opening the doors and using a fan. For 1000 cycles the attenuation of sound transmitted from outside is 57 decibels. A General Radio Sound Level Meter was used for the measurement. Each of the two inner cylinders is mounted on rubber isolation units. There is a 2-inch space containing rock wool blanket between the cylinders. The room is lined with loosely packed rock wool behind perforated metal. The anteroom has a lining of rock wool blanket lightly sprayed with aluminum paint. The over-all height is close to 8 feet, the length 11½ feet and the width 8 feet. The anteroom, which is included in the over-all dimensions above, is 8 feet high, 5 feet wide, and 4 feet deep. Each cylinder has a door of refrigerator type with rubber gaskets. The total weight of the room is 3½ tons.

Ventilation and claustrophobia are two problems which might appear serious on paper. We have been fortunate and do not worry about them. The room is mounted on a special truck. Travelling conditions have been entirely practical. By this means we were able to follow up men who were examined at the commencement of their flying training, during their flying training and at the end of their flying training. From observations made in the course of following up the men on Flying Stations, including over 11,000 hearing tests and a general view of the surveys, it is clear that during flying training, little, if any, hearing loss can be said to occur. For a period of a few hours after descent from flight, a man's hearing is impaired but no lasting impairment is observed (Fig. 2).

Audiometric Test Equipment. The development of such apparatus as would enable the known hearing acuity tests to be performed has been accomplished by the engineers of our audiometric research staff. The purpose of such apparatus was to try to standardize the method and the conditions under which audiometric tests are made. For example, some of the more common tests that might be required of the apparatus are:

1. Loudness balance—that is, comparison of subjective loudness in the two ears.

2. Intensity and range of tinnitus.

3. Pure tone threshold for any frequency from 50 to 10,000 cycles per second.

4. Variable pure tones, for pitch discrimination between ears or for the same ear.

5. Warbling—pitch variation of a pure tone in either or both ears.

6. Articulation (To be described.)

7. Equal loudness—that is, the equivalent loudness of any two tones perceived in the ear.

8. Masking—used in general in connection with any of the above-mentioned tests.

In order to perform such a variety of tests it is obvious that the equipment must be able to reproduce with the greatest degree of fidelity any frequency in the audible spectrum of 50 to 10,000 cycles per second. In addition it must be possible through the apparatus

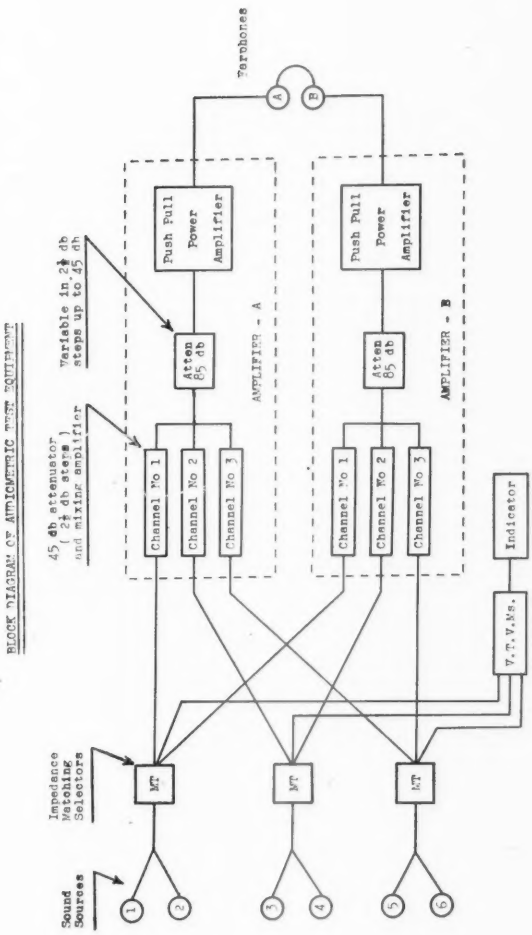
BLOCK DIAGRAM OF AUDIOMETRIC TEST EQUIPMENT
Sound Sources
Impedance Matching Selectors
MT
MT
MT
1
2
3
4
5
6
45 db attenuator (2½ db steps) and mixing amplifier
Variable in 2½ db steps up to 45 db
Channel No 1
Channel No 2
Channel No 3
Atten 85 db
Push Pull Power Amplifier
AMPLIFIER - A
Channel No 1
Channel No 2
Channel No 3
Atten 85 db
Push Pull Power Amplifier
AMPLIFIER - B
Indicator
V.T.V.Ms.
Telephones
A
B

Fig. 3.

to control by known amounts the intensity of each individual sound delivered to each ear. The various generated sounds used to perform the test must be able to be blended together to any degree in any combination and delivered to either or both ears, for example, the determination of the pure tone threshold of one ear while the other ear is masked with noise of a known intensity above the threshold of noise for that ear. In order that the true threshold will be obtained it must be evident that the sound delivered to the ears must be absolutely free of any detectable low frequency sounds or other random noise that might be generated in the apparatus itself.

The simplest way of satisfying almost all of these stringent requirements was the use of two identical audio-frequency power amplifiers incorporating non-interactive electronic mixing. Fig. 3 shows a block diagram of the plan decided upon for such an apparatus.

A maximum of six possible sound sources was felt adequate to meet all present requirements and those of the immediate future. Selection of any three of the six sources can be made by the electrical matching devices marked *MT*. The sound is here subdivided to go to either of the two identical amplifiers *A* or *B*, outlined by the broken line, which in turn excite individually the two earphones *A* and *B* used on the subject. Since the amplifiers are identical, consideration of amplifier *A* will suffice. This consists of three similar channels consisting of identical attenuators of 45 decibels' range and an electronic amplifier. These three amplifiers are combined so that there is no interaction between the channels. The combined output of all three channels is controlled by known degrees from zero to 85 decibels by the attenuator preceding the push-pull amplifier that excites the earphone *A*.

Since the highest possible degree of reproduction is imperative, only the finest quality of electrical components could be used. In addition, the elimination of noise in the earphones was one of the major problems confronting our engineers. This is appreciated especially when one considers that the subject to be examined is inside a highly treated sound room with earphones tightly coupled by large rubber cushions to the ears. It might also be drawn to your attention that one of the features of this apparatus was the elimination of a variable attenuator in the earphone circuit, something which to our knowledge no commercially produced audiometer yet available has incorporated. This helps to minimize audible clicks in the earphone which in the region of threshold may be especially misleading.

In order that the same conditions would exist each time the apparatus was used, some simple method of standardizing the apparatus was necessary. This was accomplished by making certain that the same average intensity of sound generated by the sound source was impressed on each amplifier. To measure these intensities three identical stable vacuum tube voltmeters, one for each channel, were employed. By always adjusting the intensity of the impressed sound so as to give the same indication on the vacuum tube voltmeter, it was possible to determine, for example, the magnitude of the hearing loss by the indications shown on the amplifier attenuation dials. This again is something yet impossible in commercially produced audiometers.

A brief word in respect to the sound sources, without which the apparatus is useless, is in order. The production of pure tone was accomplished by using a high quality, commercially produced audio-oscillator that is free of harmonic distortion, hum and noise from 20 to 20,000 cycles per second. Since articulation tests are most satisfactorily reproduced from recordings, the use of a turntable free of all vibration is absolutely necessary; otherwise the reproduced signal will be superimposed on the mechanical vibration set up by the driving mechanism. This requires the use of a heavy, well-balanced, level turntable driven from the rim by a belt. The motor and speed-changing apparatus are mounted separately from the turntable proper. In order to assure absolute naturalness of reproduction, the speed of the turntable must be accurate to within a fraction of a revolution per minute. Such a turntable enables an electrical reproducer with a stylus pressure of not more than one to two ounces to be used; this reduces the record surface wear to an absolute minimum.

The production of masking noise was found satisfactory when developed electronically by amplifying many fold the random ionization of gas molecules in a conducting thyatron. The reproduction of the recorded noise generated by the Bárány mechanical noise apparatus was also found satisfactory. The use of various frequency compensating networks enabled the elimination at will of higher or lower order frequency components of the noise, similar to a tone control on a radio.

In addition to the electronic equipment just considered, there is also included a tone-interrupting device consisting of a mechanically driven switch originated by the Moscow otologist, Lifshitz. This consists of an insulated disc on which there are metallic contacts

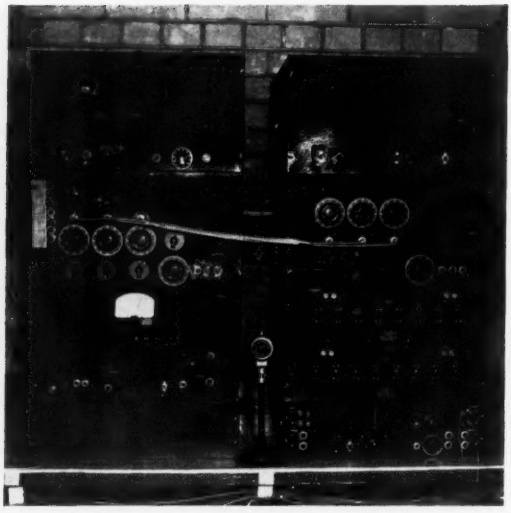

Fig. 4.—General view of audiometric test equipment.

mounted in such a fashion that a sliding make-and-break action by four brushes is possible. The speed of the disc is controlled to rigid tolerances.

The uses of this switch are more interesting than its mechanical details. The switch may be used in the determination of equal loudness of two different frequencies at two intensities in either or both ears simply by presenting the pure tones alternately to the ear. It should be pointed out that this switch is not necessarily used in conjunction with the electronic reproducing equipment previously considered. Some additional uses of the switch are the determination of the magnitude and range of tinnitus, the detection of varying threshold, and the variation in loudness balance at different intensities. The intensity of the sound is controlled by attenuators variable in one decibel steps.

The chief disadvantage from the clinician's standpoint is that when the electrical circuit is made and broken electrical transients, or clicks, are heard in the earphones, all of which makes the determination of the true threshold difficult. Electronic means of performing the same operation with a minimum of undesirable clicks is

AUDITORY TEST NO. 9

List 1-a

1. SUNSET	19. OATMEAL
2. WHITEWASH	20. WATCHWORD
3. DRAWBRIDGE	21. COUGHDROP
4. ARMCHAIR	22. DOORSTEP
5. WILDCAT	23. WOODWORK
6. BIRTHDAY	24. PLAYGROUND
7. BONBON	25. BOBWHITE
8. BLOODHOUND	26. SHOTGUN
9. SIDEWALK	27. WIGWAM
10. SHIPWRECK	28. HOTHOUSE
11. CUPCAKE	29. BUCKWHEAT
12. COWBOY	30. BASEBALL
13. DOVETAIL	31. EGGPLANT
14. EARTHQUAKE	32. EYEBROW
15. FIREFLY	33. STAIRWAY
16. AIRPLANE	34. RAILROAD
17. HEDGEHOG	35. HEADLIGHT
18. HARDWARE	36. MOUSETRAP

37. OUTLAW
38. BAGPIPE
39. INKWELL
40. BLACKBOARD
41. BACKBONE
42. NORTHWEST

Fig. 5.

now in its experimental stage and from the last report promising results can be expected. Since all of the above-mentioned apparatus is outside the room where the subject is tested a two-way communication system is used.

Figure 4 shows a view of the apparatus just considered. Starting at the top left the pre-amplifiers, compensating networks and electronic noise generator are shown. Below is one of the two identical mixing amplifiers followed by the standardizing meter and intercommunication amplifiers. At the top right the power supply for the entire assembly is housed. Below is the second mixing amplifier; following this are the attenuators used with the Lifshitz switch beneath.

ROYAL CANADIAN AIR FORCE WORD LIST NO. 1

1.	COOKBOOK	19.	BLACKOUT
2.	FAREWELL	20.	DOORMAT
3.	ICEBERG	21.	HOTDOG
4.	MISHAP	22.	GRANDSON
5.	PANCAKE	23.	OUTSIDE
6.	HORSESHOE	24.	PLATFORM
7.	TOOTHBRUSH	25.	SUNDOWN
8.	WOODCHUCK	26.	SCARECROW
9.	YARDSTICK	27.	BEEHIVE
10.	CARGO	28.	DUCKPOND
11.	EARDRUM	29.	GREYHOUND
12.	HOUSEWORK	30.	LIFEBOAT
13.	MIDWAY	31.	NUTMEG
14.	PADLOCK	32.	PLAYMATE
15.	SCHOOLBOY	33.	STARLIGHT
16.	THEREFORE	34.	WASHBOARD
17.	WHIZZBANG	35.	ALTHOUGH
18.	WORKSHOP	36.	DAYBREAK

37. FOOTSTOOL
38. JACKKNIFE
39. MUSHROOM
40. PINBALL
41. SOYBEAN
42. VAMPIRE

NOTE: The words and sequence used in this list were identical to list 2A of United States National Defense Research Council Auditory Test No. 9.

Fig. 6.

Articulation Tests. The purpose of using articulation tests in connection with audiometry as it is generally known to-day is that the determination of the threshold of hearing by means of the human voice provides supplementary data to that from pure tone audiometry. Up to the present, three different types of articulation tests have been used. The material used to make up the articulation tests is recorded in order that a definite standard of reproduction can be attained for all the tests, regardless of whom they may be used by, a procedure that is absolutely impossible in the widely used whispered voice test. The first two of these tests to be considered are more or less standard types of articulation tests, while the third is an experimental type yet to be proven practical.

ROYAL CANADIAN AIR FORCE WORD LIST NO. 5

1.	COOKBOOK	19.	BLACKOUT
2.	FAREWELL	20.	DOORMAT
3.	ICEBERG	21.	HOTDOG
4.	MISTAKE	22.	INKWELL
5.	PANCAKE	23.	OUTSIDE
6.	HORSESHOE	24.	PLAYGROUND
7.	TOOTHBRUSH	X25.	MOUSETRAP
8.	WOODCHUCK	26.	SIDEWALK
X 9.	BUCKWHEAT	X27.	AIRCRAFT
10.	CARFARE	X28.	BLACKBOARD
11.	BLOODHOUND	29.	RAILROAD
12.	HOUSEWORK	30.	SHIPWRECK
13.	MIDDAY	31.	CARLIGHT
14.	PADLOCK	32.	PLAYMATE
15.	SCHOOLBOY	33.	STAIRWAY
16.	DANCEFLOOR	34.	WASHBOARD
17.	DOORKNOB	35.	ALTHOUGH
18.	WORKSHOP	36.	DAYBREAK

37. OATMEAL
X38. WOODWORK
X39. HARDWARE
40. BAGPIPE
41. EARTHQUAKE
42. DOORSTEP

NOTE: The letter X beside a number denotes words altered from the previous list.

Fig. 7.

Considering these tests individually, the first test used was the United States National Defense Research Committee Auditory Test Number 9, prepared by the Psycho-Acoustic Laboratory, Harvard University (Fig. 5). The material used to make up this test consists of two lists of words each containing 42 familiar disyllabic spondaic words, that is, words in which both syllables are accented. Each list of words is divided into six versions, each version is subdivided into seven groups of six words. In the recording of the words, each group of six words is recorded at progressively lower intensity levels, each level differing from the preceding level by four decibels. Hence, a maximum range of attenuation of 24 decibels is possible in reproduction. Preceding each word a designating number is used. The time elapse between the test word and the designating number is

sufficient for the candidate being tested to repeat the test word. Recorded on the same record is 15 seconds of tone of 1000 c.p.s. at an intensity level equal to the average intensity level of the first group of recorded words. The purpose of this is to insure uniform reproduction by all electrical systems.

The second type of test, developed by the Royal Canadian Air Force, is similar to that just described, except that an effort to improve the selection of words was made. This test also differs in that the entire list was not subdivided and that the entire list was recorded at an average intensity level equal to the intensity level of the 1000 cycle standardizing tone (Figs. 6 and 7).

The third type of test differs from the other two tests only in that sentences as taken from the most recent Harvard word list are recorded along with a constant background noise. The intensity level of the noise equals that of the standardizing tone. The average intensity level of the sentences is such that a person with normal hearing can detect approximately 50 per cent of the key words of the sentences. The sentences are relatively simple in construction and recorded in such a fashion that enough time elapses between sentences to allow a patient to repeat the sentence.

It should at this point be drawn to your attention that the first two tests are primarily hearing acuity tests, used to determine the threshold of audibility for speech, while the third is merely a measure of hearing acuity for speech versus the normal ear under assimilated field conditions where surrounding noise is present. The latter test obviously could not be performed at threshold.

In actual practice the Harvard Number 9 test is automatic in determining threshold of audibility for speech, since the group of words are progressively attenuated, while in the second test attenuation must be introduced by the operator in the reproducing equipment to determine the same. This might at first seem highly undesirable in view of the self-attenuation of the Harvard Number 9 test. However, this disadvantage is overcome immediately when one considers that the signal-to-noise ratio remains constant in the second test throughout the entire word list; whereas, in the Harvard Number 9 test the noise always inherent in recordings remains constant, but the intensity of the recorded signal is lessened as previously described, since constant replaying can only add to the already present noise, as well as wear the sides of the recorded grooves and cause the recorded signal to become more inaudible in reproduction. Since threshold rarely falls within the first two groups of the Harvard

Number 9 test, where the signal-to-noise ratio is less significant relative to that of the following groups, obviously the increasing ratio of noise to signal can only affect the determination of the true threshold of audibility for speech. Another physical disadvantage of the Harvard Number 9 test is that the intensity of the recorded designating number relative to the intensity of the test word is too great, necessitating the ear to attenuate this sound when straining to hear the test word. The ear as in the case of other sensory organs has a delayed action in recovering from sudden shock, which obviously varies with the physical state of the patient; hence the true threshold is affected.

In an actual field survey conducted by the Royal Canadian Air Force on 250 of its personnel of all ranks and trades undergoing discharge, these tests were included as part of their final medical examination.

The tests were conducted in a sound treated room; the subject had both ears covered with similar earphones during the entire test, rubber cushions were used to assure adequate coupling of the earphone to the ear and to aid in the reduction of ambient noise. The patient was apart from the operator and the apparatus used to reproduce the test. The reproducing apparatus is referred to as the gramophone audiometer and was developed by the Royal Canadian Air Force to perform any one of the above-mentioned tests. In order to communicate with the patient a two-way intercommunication system was employed.

Of the 250 subjects tested, 191 were chosen at random, while 59 men were chosen because they showed a hearing loss in the whispered voice test.

To compare this method of testing with that of pure tone audiometry, a Maico audiometer was used under similar conditions to those for the gramophone audiometer and the frequencies considered most important in speech reception were tested, these being 512, 1024 and 2048 cycles per second.

The results of this comparative test showed a significant correlation of 0.69 between the pure tone test and the articulation test for 137 men (of the 191) of which there were 245 normal ears and 29 abnormal ears.

In the case of the 59 selected men mentioned above, in which there was 98 abnormal ears and 20 normal ears, a significant correlation of 0.85 was obtained for the same comparison.

I wish now to record briefly the result of another survey of 4687 men in which the whispered voice test and audiometric test have been completed correctly. The men were a random sample from the Royal Canadian Air Force who were being discharged, and by chance about an equal proportion of aircrew and groundcrew were included in the sample. A random sample was obtained by an order that all the men going through the discharge centre were to be given the test. A record of each test, called an audiogram, was forwarded to the Institute of Aviation Medicine. Later each of the 4687 audiograms was coded on a Hollerith card. The trend of otological opinion on hearing tests favours replacing the whispered voice test by a more exact test. Such a test is provided by the electric audiometer now accepted by otologists everywhere as a standard part of the examination of ears. The tests were carried out in partly soundproof rooms, the noise level at various times was measured in the rooms with a General Radio Sound Level Meter; levels as high as 45 decibels were recorded. Four operators conducted the tests; each of the operators belonged to the Otological Research Group and so had previous experience in operating audiometers. Five Maico D5 audiometers were used and their serial numbers were recorded. Two had the 1945 type of earphone and the other three had the previous type of earphone.

When the performance of an audiometer became suspect, a freshly calibrated replacement was sent at once from the Otological Research Laboratory at the University of Toronto. Each audiometer was checked daily. The operators took their own audiograms and when unusual audiograms were obtained with one of the audiometers, a replacement was called for and the suspect instrument went to the Otological Laboratory. The audiometer was found to withstand satisfactorily for practical purposes the demands made of it. Daily standardization of the audiometer by the operator's taking an audiogram on himself at the commencement of the day's testing and checking it with his usual audiogram sufficed for accuracy. Variation of plus or minus five decibels on a frequency necessitated calibration at the Laboratory. The test was carried out at 256, 512, 1024, 2048, 2896, 4096 and 8192 cycles per second in that order. The operator tried the man at 15 decibels for each frequency. If any frequency was missed at this level, a complete audiogram was made and he was referred for otological consultation. At the end of each week the data were collected by an umpire and forwarded to the Medical Statistical Branch of the Institute of Aviation Medicine. The operator recorded the results of the test on a separate

form for each man with the man's number, rank, trade, time of test, length of service in months, the date of the test, the serial number of the audiometer used and the operator's initials. The following data were coded directly on the form: the serial number allocated to each man's form, his trade as aircrew or groundcrew, his length of service in months, the results of the hearing test, the worse hearing at any frequency on the right ear, the same on the left ear, the same on either ear, the results of the audiogram as "pass" or "fail" for each of the seven hearing standards and the audiometer's serial number.

By the results obtained we found the most difficult standard to be at the level of 20 decibels at 256, 512, 1024, 2048 and 4096 cycles per second. Twenty-two per cent of the aircrew, 33 per cent of the groundcrew failed this standard; 78 per cent of the aircrew and 67 per cent of the groundcrew passed this standard. The 20-decibel level is the upper limit of the zone of normal hearing for young adults as found in the Bell Telephone and United States Bureau of Public Health surveys with audiometers. If the results of this survey are compared with data on hearing tests elsewhere in the literature, the fact that the Royal Canadian Air Force was making a field test, not a laboratory test, should be remembered. 8192 cycles per second was tested, but was omitted from the standards because the hearing above 4096 cycles per second is not important to service personnel. Agreement was general on including one of the two frequencies 2896 and 4096 in all standards. The results of this survey have been useful in selecting a hearing standard because the "pass-fail" percentages have been determined for each standard on Royal Canadian Air Force personnel The aircrew "pass" percentages are probably higher than would be obtained on recruits. Aircrew are well-trained men, apt in taking all kinds of tests. Groundcrew are less trained in this sense of the word. It would be rash to examine these standards in the light of reports by civilian organizations whose equipment and testing conditions were different from the Royal Canadian Air Force set-up.

The same number of men were subjected to a whispered voice test performed by a medical officer just prior to the audiometric examination. The whisper test was designed on the simple idea that sound diminishes in the same way as a beam of light when travelling farther and farther away from the examiner's mouth. The idea is only right when the speaker and the listener are in the open air and far enough from buildings to prevent the possibility of echoes occurring. If an echo occurred from a near-by reflecting surface, it

would arrive at the ear so soon after the direct sound that no distinction would be apparent. It would not be perceived as an echo by the ear but as a part of the apparent loudness of the direct sound. This is what happens in a room when the whisper is heard more loudly than at the standard twenty feet in the open air. The effect takes place when the ear happens to be in the right position to catch the reflected sound. The narrow tunnels at present used for whisper tests reflect sounds in the same way beams of light are caught and internally reflected again in a prism, a veritable whispering gallery.

Another drawback is the variation in the loudness of different speakers' whispering. As a basis for comparison, personnel who failed either one or both tests were separated into three groups in accordance with the criteria laid down for "pass" and "fail".

Group 1. Failed the whispered voice test and passed the audiometric test.

Group 2. Passed the whispered voice test and failed the audiometric test.

Group 3. Failed the whispered voice test and failed the audiometric test.

The findings were as follows:

1. There were no failures in Group 1, that is, failed the whispered voice test, passed the audiometric test.

2. Of the 4687 men, 4198 (90%) passed the whispered voice and audiometric tests; 435 (9%) passed the whispered voice test and failed the audiometric test and 54 (1%) failed the whispered voice test and also the audiometric test.

The following are a few pertinent facts secured from analysis of the data compiled on the 489 men who failed the test. Of those who failed the whispered voice and audiometric tests and were consequently referred for consultation the findings were:

1. One half of the men referred (50%) recorded a positive history of previous ear trouble—244 cases positive, 245 cases negative.

2. In the group which passed the whispered voice test and failed the audiometric test, 227 (52%) recorded a negative history and 208 (48%) a positive history; in the group which failed both the whispered voice and audiometric tests 18 (33%) recorded a negative history and 36 (67%) a positive history.

3. Of the 489 physical examinations 335 (69%) were negative and 154 (31%), positive.

4. Of the group which passed the whispered voice test and failed the audiometric test 304 (70%) were negative and 131 (30%) positive, while in the group which failed both the whispered voice and audiometric tests 31 (57%) were negative and 23 (43%) positive.

To recapitulate

1. No one in this group who passed the audiometer test failed the whispered voice test.

2. Nine per cent of the group failed the audiometric test and passed the whispered voice test.

3. One per cent failed both tests.

4. Of the group who failed one or other of the tests and were referred for consultation, 50% recorded a history of previous ear trouble and 31% on examination had positive findings in the ear.

5. This survey was carried out on a select group and the results probably will not compare with a civilian group.

6. The audiometer in this survey again showed its practicability and durability under constant use.

CONCLUSIONS

1. The technique of the United States Bureau of Standards for calibration of audiometers has been duplicated and carried out in the Laboratory.

2. The development of such audiometric test equipment permits the carrying out of all the audiometric tests described and enables the Laboratory to carry on a recognized program of otological research.

3. Some surveys have been described and analyzed.

4. The correlation between pure tone audiometry and articulation tests is significant.

5. The audiometer has been shown and proved to be superior to the whispered voice test for testing hearing in the Services.

6. A standard for Armed Force personnel is given and merits consideration.

In conclusion we subscribe to the general recommendations which were determined as a result of the meeting of the joint services held in New London, Connecticut, June 1945, at a conference on sound; namely:

1. Joint specifications for audiometers and rooms for audiometry should be established. These specifications should be written in as much detail as possible.

2. Joint standard audiometric testing procedures should be established in as much detail as possible.

3. Service training schools for audiometricians should be established.

4. Finally, audiometric criteria for specific service jobs can probably be set up in many cases.

The author and his associates, Flight Lieutenant R. W. White, W. E. Hodges, B. A. Sc., Flight Lieutenant K. B. Smith, Squadron Leader K. McAskile wish to express their thanks to Dr. E. F. Burton, Professor of Physics, the University of Toronto, Air Commodore J. W. Tice, Director of Medical Services, the Royal Canadian Air Force, and the Committee of Aviation Medicine of the National Research Council, Canada, Wing Commander W. R. Franks, Officer Commanding the Institute of Aviation Medicine, Royal Canadian Air Force, Toronto.

We also wish to express our appreciation to Dr. Beranek and Dr. Nichols of the Cruft Laboratory for advice and the apparatus lent to us, and to Dr. M. H. Lurie for his invaluable help.

MEDICAL ARTS BUILDING

TORONTO, CANADA.

LXXV

EXPERIMENTAL AND CLINICAL OBSERVATIONS REGARDING THE NASAL VASOCONSTRICTOR ACTION OF OENETHYL AND EA-83

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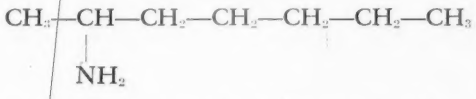
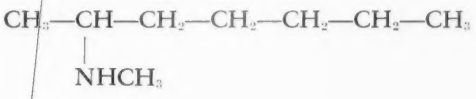
Notwithstanding the considerable number of vasoconstrictor drugs which have been used, or suggested for use, in the treatment of nasal congestion the search still goes on for compounds which may possess some advantage over the preparations which are already known. We are therefore presenting observations which we have made with reference to two new straight chain synthetic compounds, Oenethyl[1-5] (or EA-1) and EA-83 (2-methylamino-6-hydroxy-6-methyl heptane).[6]

Proetz[7, 8] has already carried out extremely interesting and valuable work with another aliphatic compound, Tuamine or 2-amino-heptane which has the following formula:

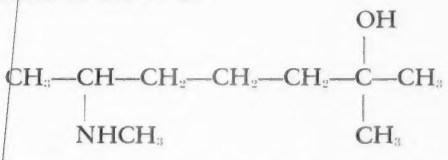


Kohlstaedt and Page[9] have also studied the cardiac action of this drug.

The formula for Oenethyl (EA-1) is as follows:



And the structure of EA-83 is:



From the Department of Pharmacology of the University of Cincinnati Medical College, Cincinnati, Ohio.

Both Oenethyl and EA-83 are colorless, volatile fluids which readily form salts with a number of acids and some of these salts are very suitable for experimental or clinical work. In the case of each drug only the racemic form has so far been made. Both drugs exercise very extensive general systemic actions which are mainly sympathomimetic in character but which vary considerably in detail.[1, 6] In this paper we deal only with the action of these compounds in the nasal walls, both in animals and in man.

In the animal work we have carried out two general types of experiments. These depend on the intravenous or the local (intranasal) application of the drugs. In the animal experiments we have used anesthetized dogs and a special technic[10] by which we have closed off the posterior nares by pressing the soft palate back against the posterior wall of the nasopharynx with a sponge rubber ball on the end of a rod which is passed into the mouth. The rod is held firmly in position by a clamp which passes around the rod (in the dog's mouth) and around the upper jaw (nose) outside the mouth. The clamp is made in two parts which are held together by butterfly nuts which permit the clamp to be adjusted firmly for any size dog. The front end of the rod rests firmly against the upper middle incisor teeth. Thus the soft rubber ball pushes the soft palate against the posterior nasopharyngeal wall and makes that end of the nasopharynx airtight. By means of another special clamp attached to the end of the rod which protrudes out of the mouth two short tubes are held firmly (airtight) in the anterior nares. A little petrolatum is used to insure a good tight connection between the tubes and the nostril walls. These two short tubes are connected by means of a Y-tube and rubber tubing to a sensitive tambour which writes upon a smoked drum. Thus changes in the air volume in the (closed) nasopharynx will be directly recorded on the drum by the tambour tracing which reflects any shrinking or swelling of the nasal walls.[11] Blood pressure has been recorded with a mercury manometer and the respiration, with a tambour connected by means of a side tube to the tracheal cannula.

Figure 1 shows a typical tracing illustrating the action of Oenethyl (EA-1). The dose injected into a femoral vein was 0.333 cc. of a 10 per cent solution of the hydrochloride salt. It will be seen that the systemic blood pressure soon rose about 100 per cent above its normal level. Correspondingly the nose record showed a marked drop downward indicating a profound constriction of the nasal vessels with great shrinkage of the nasal walls. This is by all odds the quickest and surest way to produce a maximum constriction

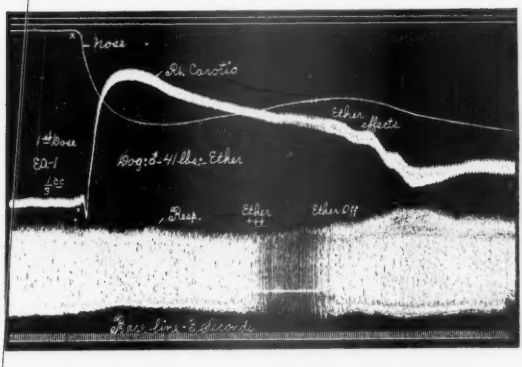


Fig. 1.—From above down intranasal volume (nose) right carotid pressure (mercury manometer), respiration (tambour connected to side tube of tracheal cannula) and base line (zero blood pressure) and 3 second time interval. Drug injected into femoral vein. This tracing is continued in Figure 2.

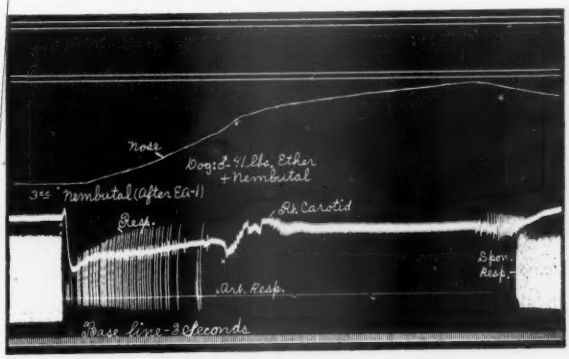


Fig. 2.—Continuation of Fig. 1.

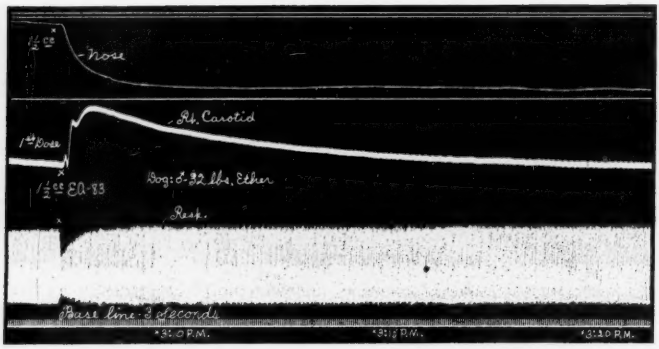


Fig. 3.—This tracing shows the effect of an injection (1.5 cc. of 10 per cent solution) of EA-83 into the femoral vein. Note the marked and lasting constriction of the vessels in the nasal walls as shown by the downward movement of the nose (tambour) record.

of these vessels. Apparently this method has been used in some instances in the treatment of hay fever with at least one other drug. Fig. 1 also shows two other features which we wish to emphasize. These are the long duration of the nasal constriction (which even increases beyond the end of the tracing) and the failure of an excess of ether (which markedly slowed the respiration) to cause more than a slight relaxation of the nasal constriction. Excess ether and nembutal usually dilate the nasal vessels.[11] This shows the tenacity with which EA-1 prolongs the vasoconstriction. There are no irregularities of the heart beat visible in the blood pressure tracing here even though the pressure is doubled, but any drug which abruptly causes such a great rise in pressure as that shown in Fig. 1 must be expected, at least in some cases, to produce cardiac irregularities from carotid sinus reflexes, or direct (or sympathetic) heart stimulation.

Figure 2 is a continuation of Fig. 1 but was made an hour or more after Fig. 1. It will be noted that the constriction of the nasal vessels had continued at practically the maximum limit. In this record an effort was made to produce a relaxation (dilatation) of these vessels by injecting a large dose of nembutal (3 cc.). This produced a profound effect on both the respiration and the blood pressure but also, at a slow rate, caused an almost complete relaxation of the nasal vessels. Presumably the nembutal exerts not only a

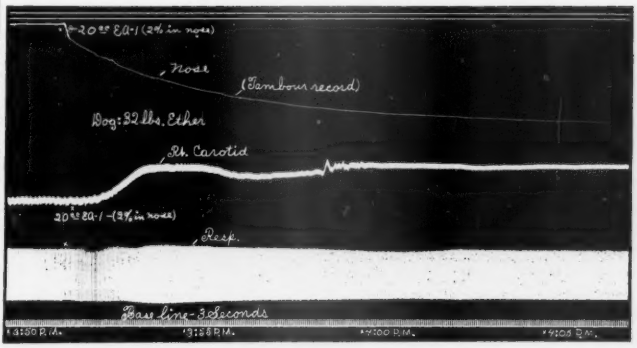


Fig. 4.—In this experiment 10 cc. of 2 per cent solution of Oenethyl hydrochloride solution were injected into each nostril and the nasal vasoconstriction (nose-tambour tracing) resulting is shown in the top record. Note also the slow progressive rise in blood pressure as the drug is gradually absorbed from the nasal cavity. This tracing is continued a Fig. 5.

central depressant action but also a direct weakening action on the muscle fibers of the vessel walls while the EA-1 appears to act on the myoneural junctions of the sympathetic nerves in these vessels. The record shows the opposing actions of these two drugs on the nasal vessels.

Figure 3 shows the marked and prolonged vasoconstriction of the nasal vessels produced by an injection of EA-83. It seems probable that, at least in dogs, this drug may not constrict the nasal vessels so vigorously as does EA-1. But it is not now possible to say which of the two may be more satisfactory for clinical use, for the general toxicity and side actions of the two drugs vary considerably. And some slight difference in the rate of local absorption, systemic or cardiac action, or local irritation might easily tip the scales in favor of the one or the other. However, it seems probable that the immediate penetrating power into mucous membranes on local application may be a little greater with EA-1 than it is with EA-83.

This latter point is illustrated in Fig. 4. In this experiment the same technic and apparatus was used as in the preceding experiments, but in this case the Oenethyl solution was injected directly into the nasal cavity by means of two long syringe needles which were inserted through the wall of the rubber tubing and through the lumens

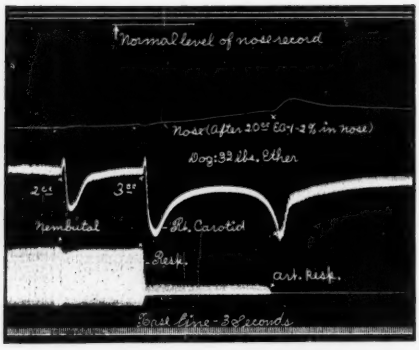


Fig. 5.—Continuation of Fig. 4. The nasal vasoconstriction continued, probably at the maximum limit. Here an attempt was made to determine whether or not Nembutal (two intravenous injections, 2 cc., 3 cc.) would bring about a relaxation of the nasal vessels. Only a slight and rather evanescent relaxation occurred following these large doses.

of the short tubes in the nostrils. By this procedure a large volume of two per cent solution was injected (10 cc. into each nostril) directly into the closed nasal cavity. The tambour was disconnected from the rubber tubing for a few seconds just as the injections were made, so that the filling up of the nasal cavity with the solution and the consequent displacement of air in the cavity would not change the tambour record. As soon as the solution was injected, the tambour was immediately reconnected and the nasal vascular constriction began to be recorded promptly as the drug started to act. This is a more vigorous method of applying drug solutions directly to the nasal membranes than is the clinical use of drops, but the principle is very much the same. In this case we recorded the slower but very lasting and intense constriction of the nasal vessels as shown by the tambour tracing. This tracing also shows what is perhaps an even more striking phenomenon in the slow, steady and persistent rise in blood pressure which was soon initiated by the systemic absorption of the drug from the nasal cavities. This same type of rise in blood pressure may also be obtained after intramuscular injection of either of these drugs, and this action should be useful in resisting circulatory collapse. This tracing shows the blood pressure rising slowly over a period of about 15 minutes and this rise might persist for two hours or more. In man the nasal constriction is also very persistent.

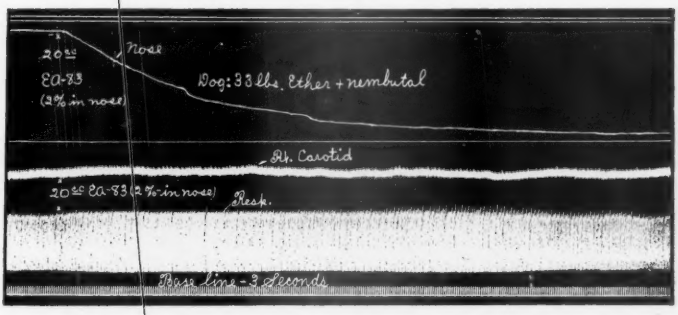


Fig. 6.—In this experiment EA-83 (10 cc. of 2 per cent solution) was injected into each nostril. Nasal vasoconstriction began at once and progressed rather slowly, probably to the maximum limit. The systemic blood pressure did not rise and this perhaps indicates that systemic absorption from the nasal mucosa is less than that which occurs with Oenethyl- (see Fig. 4). This record is continued in Fig. 7.

Figure 5 is a continuation of Fig. 4 but was made about 50 minutes later. The blood pressure was still about 20 per cent above the initial level and the nasal constriction was probably at the maximum limit. An attempt was then made to see if the nasal constriction could be relaxed by injection of nembutal solution.[11] Two injections (2 cc.-3cc.) produced only a slight indication of any relaxation even though the two injections caused complete stoppage of the respiration and artificial respiration had to be administered to continue the experiment. This shows the extreme persistence with which EA-1 maintains the vasoconstriction. Several minutes later natural respiration returned but the nasal vessels remained constricted.

Figures 6 and 7 illustrate an experiment exactly similar to that shown in Figs. 4 and 5 with the exception that in Fig. 6 the drug injected into the nasal cavities was EA-83 instead of EA-1. The EA-83 also brought about a very profound constriction of the nasal vessels as shown by the downward curve of the "nose" record. Approximately one hour after Fig. 6 was recorded an attempt was made to produce a relaxation of the nasal vessels by the intravenous injection of a large dose of histamine[11] solution (Fig. 7). This caused a marked and persistent fall in blood pressure with slowing of the respiration, but only a slight and evanescent dilation of the nasal

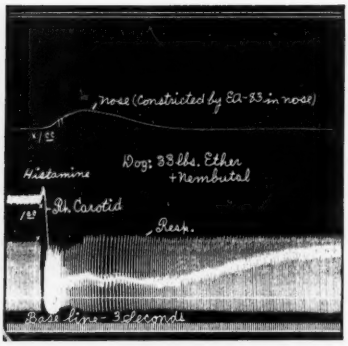


Fig. 7.—Continuation of Fig. 6. Here an attempt was made to see if histamine would overcome the vasoconstriction produced by the EA-83. Only a slight, temporary dilatation was produced by the histamine. Possibly the intense vasoconstriction brought about by the EA-83 prevented much of the histamine from reaching the finer nasal vessels.

vessels occurred. This again indicates the persistence of the constricting action of these drugs on the nasal vessels.

We have not attempted so far to study the action of the vapors of the volatile free bases of these drugs on the vessels of animals. But from experiments on man we believe that constriction would readily be produced.

EXPERIMENTS ON MAN

In order to make a quantitative study of the action of these two drugs on the nasal vessels in man we have used a special device which is a modification of the original apparatus used by Sternstein and Schur[12] and later modified by Butler and Ivy.[13, 14] This apparatus is rather complicated but its action may be simply explained in the following manner. If one imagines a Y-tube with the same inside diameter in each limb and then considers that air at the rate of six liters per minute is being drawn through the tube and out the straight (perpendicular) limb at the bottom by means of an electric pump with the air current being regulated by a flow meter, then air will be entering each of the short limbs at the rate of three liters per minute. If now one of the short limbs of the Y-tube be connected to one nostril of the subject by means of a rubber tube which carries a short piece of glass tubing with a bulbous opening for insertion

(with a little petrolatum) into one nostril of the subject, and a draft gauge (inclined glass tube half filled with water) be connected by rubber tubing to the free (third) limb of the Y-tube, then it can be seen that air which is drawn out of the one nostril of the subject may just have passed into the other nostril if the subject keeps his mouth tightly closed and holds his breath absolutely still. The draft gauge connected to the third limb of the Y-tube will register the amount of resistance which the two nasal passages and the nasopharynx offer to the passage of the air from the outside into the open nostril, through the choanae and the nasopharynx and out through the opposite nostril, that is, it measures the congestion or shrinkage of the nasal walls. The draft gauge is really made up of a glass cylinder half filled with water, while an opening at the lower end of the cylinder is connected directly with the inclined glass tube so that the level of the water registers at about the middle of the cylinder and also at the middle of the inclined tube. The top of the cylinder is connected by means of a stopper, a short piece of glass tubing and rubber tubing to the third limb of the Y-tube. Thus it can be seen that drugs which increase or decrease the vasoconstriction within the nose will cause a fall or a rise in the draft gauge reading because air will pass more or less readily through the nasal passages. These changes in the air pressure readings on the draft gauge will continue so long as the action of the drug persists. Thus swelling of the membranes in the nose (obstruction) will mean that the pump will exert more negative pressure in order to draw through the six liters of air per minute and this increased negative pressure in the upper part of the water cylinder will cause the water level to rise a short distance in the cylinder and this will cause the level of the water to fall through a much longer space in the small-bored inclined tube of the gauge. It is this fall in the meniscus in the inclined tube which gives the readings, from which the graph shown in Fig. 8 was made.

Healthy adults free from upper respiratory infection and nasal obstruction were used. Six subjects were used for Oenethyl and eight for EA-83.

Each of the two drugs studied was in the form of a two per cent aqueous solution used in the form of a spray. No aromatics were added as Butler and Ivy have shown that the presence of volatile substances may alter the efficacy of a vasoconstrictor.[14]

The rate of air flow was regulated by the flow meter and adjusted to six liters per minute in all cases. This was taken as an arbitrary value and much higher rates were avoided, since at those higher

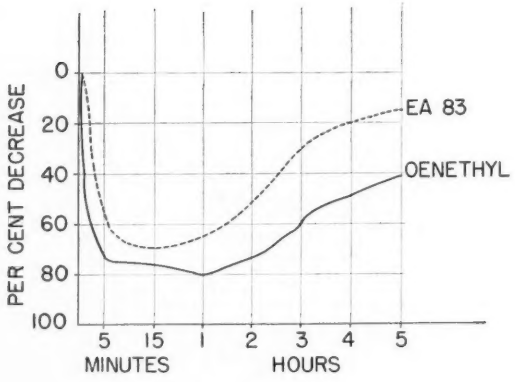


Fig. 8.—Graph showing curves plotted from the percentage readings from the inclined tube in the experiments on patients. The downward dip of the curves shows the increased patency of the nasal passages brought about by the vasoconstriction when EA-83 or Oenethyl was sprayed into the nostrils.

rates the subject could feel the flow of air and it was feared that the sensitive mucosa might be responsive to the air flow. The degree of obstruction encountered by the air in flowing through the nasal system could be read by changes on the draft gauge which was calibrated in inches of water. It was necessary to "educate" each subject in the manner of completely holding his breath while his mouth was closed. It was also necessary to test each subject several times before administering the drug in order to assure complete cooperation. Readings were taken with the nasal olive glass tip alternately in each nostril. Three readings were taken on each side and an average of these six was determined. A pretreatment (base) line (marked "O" in Fig. 8) was taken, then the nose was sprayed and readings were taken at intervals of 1, 2, 3, 4, 5, 10, and 15 minutes and every hour for 5 hours. Subjects were directed to sit for two to three minutes with head erect before readings were taken. Changes in the position of the head, tight collars and exercise were found to change the readings (increased nasal obstruction due to venous congestion). It was found advisable for one person to hold the olive tip in place in the nostril while another read the gauge.

Spraying was accomplished by a DeVilbiss type of atomizer with compressed air serving as the spraying force. The subject's head was again maintained in the erect position during the spraying

for the reason given above. The pressure of the compressed air was 30 pounds. The spray tip was placed just within the nasal vestibule, and each nostril was sprayed three times for a duration of one second at each spraying. The nostrils were sprayed alternately.

Results. In all cases the change of degree of obstruction is a negative per cent (decreased obstruction). The per cent change is based on the pretreatment reading or base line. In Fig. 8 the average per cent change (decrease) is plotted for Oenethyl and EA-83.

Oenethyl and EA-83 both are active vasoconstrictors when sprayed on the nasal mucosa. It can be noted from the graph (Fig. 8) that both drugs act quickly in decreasing the degree of nasal obstruction in normal adults. Moreover each is free of any initial increase of obstruction (congestion) or of any obstruction increase during a five-hour period. In fact each drug maintained vasoconstriction during the entire test period. Two of the EA-83 subjects were tested at the end of six hours and had not then quite reached the base line.

Of the two drugs Oenethyl appears to be the more effective both in speed of action and in degree of action on the nasal vessels. At the end of five hours Oenethyl maintained a decrease of obstruction slightly in excess of 40 per cent of the base line reading.

Clinically the drugs proved to be well accepted by the subjects. There was no degree of burning or noticeable sensation of constriction subjectively. There seemed to be no generalized effects that could be noted by the subjects.

Although no detailed study was made of patients suffering from upper respiratory infection, Oenethyl proved very satisfactory in relieving congestion in patients with acute rhinitis and sinusitis. This observation was made by one observer (S) working in the Ear, Nose, and Throat Clinic of the Cincinnati General Hospital.

SUMMARY

Two drugs, Oenethyl and EA-83, are discussed and shown to be active vasoconstrictors of the vessels in the nasal mucosa. In animals this occurs both after intravenous injections and after local application of solutions in volume in the nasal cavities. In man entirely comparable results are obtained when either drug is applied locally (spray) to the nasal mucosa of normal individuals. Both drugs are active in man over a period of five hours, as shown by quantitative studies. Oenethyl is probably the more active of the

two in relieving nasal congestion, and it proved effective in a number of patients suffering from acute rhinitis and sinusitis. Both drugs, and especially Oenethyl, are worthy of further study in this field. We have not noticed any bad side effects in the nasal action of these drugs in man.

UNIVERSITY OF CINCINNATI
COLLEGE OF MEDICINE.

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LXXVI

EVALUATION OF ALLERGEN DIAGNOSIS

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The diagnosis of the specific substance or substances in any case of hypersensitivity is a relatively modern and not entirely accurate procedure. With the recognition of the allergic nature of several syndromes such as asthma, certain forms of rhinitis, eczema, urticaria, migraine, functional gastro-intestinal disturbances, and a variety of minor ailments, details of the cause-and-effect relationship are paramount. In a number of instances the affected individual is fortunate enough to have made his own observations and conducts himself accordingly. The investigating physician likewise is able to come to probable conclusions in many instances from the patients' history and his knowledge of types of reaction and the nature of reactions. In either event, however, observation and interpretation must be corroborated by some specific diagnostic test to justify a reasonable therapeutic plan.

According to our medical historians, the earliest experiment of this nature took place in 1835 when pollen was applied to the broken skin and the nasal mucosa of a physician who suffered from seasonal coryza. Since the specific cause was known to be ragweed, the test definitely established the cause-and-effect relationship. Later in 1873 this earlier informal procedure was applied in the testing of hay fever patients with various pollens. Great impetus to this form of diagnosis occurred in 1909 as a ramification of work being done with tuberculin skin sensitiveness. The skin scratch test with inhalant allergens was adopted for the detection of probable excitants of the allergic states by 1912. About the same time the intracutaneous method, employing solutions of various allergens, came into prominence.

Skin testing by the scarification technique has become a standard diagnostic procedure in all forms of allergic disease. Its efficiency, aside from inhalant allergens where it is highest, is not sufficient to justify complete confidence. Actually many investigators contend that skin testing with food allergens is no more than 50 per cent accurate at best. The intradermal method is more accurate but it

has the disadvantages of being somewhat painful, possibly giving rise to untoward systemic reactions, and being restricted in universal employment because the number of skin injections must be limited at any one sitting. The conjunctival test, although highly informative in cases of nasal and paranasal allergy, is naturally restricted because of anatomical limitations. Passive transfer testing is very valuable but here again practical difficulties are encountered in getting not only willing but also cooperative recipients. All these methods so far enumerated are based on the scientific duplication of at least one physiological change occurring in most allergic states: namely, capillary dilatation and increased capillary permeability with extravasation of blood elements into the tissues. The changes in the cellular elements of the blood, such as eosinophilia, have long been recognized as important in the diagnosis of the allergic state. The total leucocyte count and the lymphocyte-polynuclear relationship have been applied clinically as diagnostic criteria in the "leucopenic index" method of testing. In this method there is a great deal of laboratory work involving the prominent factors of errors in calculation and cell identity. Since well over a hundred allergens should be considered in practically every case the cooperation of the patient may be strained beyond his endurance. Hence the elaborate and interesting leucopenic index is relegated to a corroborative status.

While studying the effects of certain physical and mechanical respiratory impediments on the eosinophile content of circulating blood, it was found that the addition of histamine induced characteristic changes. Shed uncoagulated blood of experimental animals and of humans was smeared thickly on glass slides treated with supravital stains. A drop of 1:100,000 solution of histamine phosphate was added to the preparation and sealed in a hot box. There was a sharp rise of eosinophilic staining leucocytes in the preparation. This change was characterized not only by alteration of the staining affinity of the granulocytes but also by a marked increase in the size and coarseness of the nuclear particles. Changes occurred only in those polymorphonuclear neutrophiles which had three or less segments in the nucleus, in other words the younger forms. It was further noticed that these changes occurred only in those blood specimens taken from experimental animals which had been previously traumatized or used in laboratory work involving some substances, such as drugs, foreign to the animal's normal environment. On checking the source of the human specimens it was found that in each instance the individual had an allergic state himself or gave a family history of the diathesis. Four of these persons were medical students who knew

the cause of their hay fever, ragweed. They became the subject of further study.

When a drop of a 1:100,000 dilution of ragweed pollen extract was added to the stained blood preparation, the eosinophile content rose from 2 to 9 per cent within a few minutes. These original studies were carried out during the month of January 1939. The following September three of these students had mild, moderate, and severe hay fever, respectively. None of the three had been hyposensitized. The differential leucocyte counts showed, in the order named, 4 per cent, 9 per cent, and 16 per cent eosinophiles. The addition of a drop of either the 1:100,000 ragweed dilution or the 1:100,000 histamine solution produced a rise to 8.5 per cent, 16 per cent, and 22 per cent, respectively, in vitro. The fourth student had received preseasonal and coseasonal graduated doses of ragweed extract. In this case the same experiment caused only an increase to 2 per cent over the basic 1 per cent eosinophiles. However, when the concentration of the pollen extract was increased to 1:10,000 or the histamine 1:100,000 a further rise of 6 per cent was obtained. In the three cases of active hay fever the blood cell changes did not occur after a sufficient amount of ephedrine or a similar pharmacological agent had been administered to practically obliterate symptoms.

The facts that changes in blood can be provoked independent of the controlling body influences within a few minutes and that the leucocyte granules changed not only in their chemical affinity but also morphologically, convinced us that further attempts along chemical lines might facilitate allergic diagnosis. This method of inquiry was employed in 24 cases of known inhalant allergy with perfect results. A small number of atopic eczemas in children (6 cases) which were known to be caused by milk or egg in the diets were studied in the same way with uniformly accurate results. The allergen reagent used was a 1:5000 dilution of milk protein in the milk sensitive patients and a 1:10,000 dilution of egg in the egg sensitive patients. Here again, as in the other methods of testing, the procedure is impractical for routine use. For example, it would take constant observation of blood preparations under the microscope to determine even a few antigens without the investigator's vigilance being overtaxed to avoid possible errors in technique and calculations. Finally, because of previous work done on blood titres of precipitins and agglutinins and the contradictory evaluations of these determinations in blood sera and plasma of allergic individuals, a modification of this principle was investigated. Using first serum and

later plasma it was found that the addition of either pollen extract or histamine solution caused a turbidity which could be seen macroscopically in many instances and in higher dilution by means of the nephelometer in all. For purposes of extensive testing with a large number of allergens high dilutions of sera or plasmas are necessary and to carry out such a program modifications were developed which form the basis of this clinical report.

During the past six years a group of 2164 patients who had one of the major allergic disturbances was studied. Each patient was observed for from two to five years to be certain of accuracy. They were all of the white race, between 8 and 34 years of age, of both sexes, of all ordinary occupations, and all residents of New England, mostly of greater Boston. In each instance the procedure and the ultimate goal were the same: namely, to limit the cause of each particular allergic syndrome to one outstanding etiologic factor. Depending upon the clinical substantiation of the laboratory diagnosis in each case the individual study was considered a success or a failure.

Technique. Five cc. of blood is aspirated from the aseptically prepared anticubital vein with a sterile needle and syringe. This is immediately hemolyzed with an equal volume of distilled water in a test tube, which is tightly stoppered and refrigerated at 5° C. or as close to it as possible. Because of the possibility of confusion in reading the tests, it is our policy to have patients abstain from any medication for one or two days before a blood specimen is taken. Since it is probably a colloid phenomenon any extraneous clinical influences are not only undesirable in general but also specifically, as noted elsewhere with regard to ephedrine and similar compounds. This precaution also applies to the sulfonamides since they lead to methemoglobin formation and interfere with accurate dilution of the hemolyzed blood.

The hemolyzed blood is centrifuged to separate out cell fragments and cellular elements. The clear supernatant liquid is decanted and enough distilled water added so that compared with a hemoglobin standard it is colorimetrically the equivalent of 1.3 grams per 100 cc. In this way one need not be concerned with the corrections otherwise necessary if there is an anemia. Furthermore, a uniform dilution of non-cellular elements is available in sufficient quantity for about 200 tests. No preservative is required since the preparation is refrigerated and used within a reasonable time.

The allergen medium is made up in bulk and kept refrigerated. For convenience the prepared medium is placed in small glass vials

2.5 cm. long, 0.5 cm. in diameter, with a capacity of 0.5 cc. A number of tubes for each particular allergen are prepared at the same time and can be stored for several weeks before use without deterioration. Various substances have been used as medium bases, gelatine, agar, glycerinated gelatine, and glycerite of starch. Each of these has its limitations and at the present time the best base appears to be a vegetable albumose. This is taken in the dry state and a sufficient amount of a 1:50,000 allergen solution added to bring it into a liquid state. Two cc. of this preparation is then placed in each glass vial to be stored for immediate or later use and refrigerated. It rapidly solidifies on standing a half hour. The method of Coca has been employed for the preparation of most allergen solutions. Special methods are used for the pollens, dusts, animal epidermals and bacterial protein extracts. To prevent drying of the media if they are not to be used within a few days, the refrigerator must be carefully humidified and the tubes covered with moistened filter paper or a blotter.

Two cc. of the diluted hemolyzed blood is superimposed on the prepared medium in the tubes and the set of each individual's tests placed in an incubator at the same time. They are kept at 37° C. for several hours, usually overnight. Readings are then made by use of the nephelometer. A positive reaction has been interpreted by us to be a zone of density at the junction of the blood dilution and the medium. A control, containing untreated medium and a portion of the untested blood dilution, is used for comparison. A second control consists of untreated medium and distilled water.

Obviously this method entails considerable work in the preparation of tubes and in care of the glass. At the present time experiments are under way to reverse the process; that is, using the untested blood in the medium solidified in petri dishes. These may be spotted with allergen dilutions so that 32 to 64 tests may be done on each plate.

Since the histamine reaction in tissues so closely resembles the allergic and since changes occur in the cellular and non-cellular elements of the blood as described above, all blood specimens were routinely tested with histamine-containing media. Of 2164 patients a positive reaction to histamine *only* was obtained in 139 cases, or 6.4 per cent, of the whole group. Fifty-four additional histamine reactors, or 2.5 per cent, had also a positive test for some extrinsic factor as a complication of our laboratory diagnosis. One hundred sixteen of the first sub-group of histamine reactors, or 89 per cent,

obtained from marked to complete relief by hyposensitization with histamine solutions. In the second sub-group (54 cases) identical treatment together with avoidance of the indicated extrinsic factor proved valuable in 42 patients or 77 per cent of the group. A single course of histamine hyposensitization is not a permanent cure and must be repeated. In our experience these intervals varied from a month to a year and in several instances continuous histamine therapy was necessary for control of the patients' symptoms. Here a plan of treatment has been established similar to the perennial program of pollen hyposensitization.

In the large group where extrinsic factors *only* were established by our laboratory findings, the symptoms of 1732 patients of the 1963, or of 88 per cent, were effectively controlled as long as they cooperated by following rigid regulations for the avoidance of the offending substance. Out of this group only cases of bacterial or inhalant hyperergy were treated "actively" by specific parenteral hyposensitization. Institution of the "passive" regime of allergic control necessitates in many instances careful education of the individual concerning not only the composition of his diet but also the ultimate nature of its ingredients. Compliance or failure in this respect decides the issue, clinically and statistically. This is particularly true of primary foodstuffs such as wheat, egg and milk, which are universally the ingredients of so many dishes. Here the science of the dietitian, the art of the epicure and the mental toil of the allergic patient must be sublimated.

	CASES	PER CENT
Total number cases	2156	
Total number histamine reactors (only)	139	6.4%
Histamine desensitization successful	116	89%
Histamine desensitization unsuccessful	23	11%
Histamine factor plus extrinsic factor	54	2.5%
Symptoms successfully controlled	42	77%
Symptoms not successfully controlled	12	23%
Total number reacting to extrinsic factors (only)	1963	91.1%
Symptoms successfully controlled	1732	88%
Symptoms not successfully controlled	231	12%
TOTALS		
Successful Cases	1890	87.7%
Unsuccessful Cases	266	12.3%

In tabulating the list of extrinsic factors it has been impossible to present any orderly grouping of the offending substances. No common denominator of chemistry, biology, physics, nutritional needs, or frequency of use was adequate as an index. According to the incidence of reactions they have been listed in the arbitrary fashion: foods 69.4 per cent, inhalants, 12.8 per cent, bacterial proteins 11.7 per cent, beverages 1.9 per cent, clothing materials 1.4 per cent, and a miscellaneous group of 2.8 per cent which includes tobacco and the condiments. In the 231 failures (12%) of the extrinsic group the breakdown of figures is roughly the same as that for the successful except for the higher incidence of laboratory findings of bacterial hypersensitiveness.

The food group is interesting in that the vegetable-fruit, the cereal, and the fish sensitivities were most frequent, the meats least and dairy products and poultry intermediate. Comparison of these figures with those published reports of many investigators on skin tests are not entirely satisfactory but close enough to confirm the general accuracy of all methods as far as they go.

CONCLUSIONS

1. A method for routine study of allergic problems is reviewed. This method necessitates a minimum of discomfort for the patient, is entirely objective, and does not interfere with symptomatic relief pending etiologic diagnosis.

2. This review suggests further simplification and application of the method.

3. It offers through finer diagnosis an easier existence for those who have been overwhelmed heretofore by staggering lists of positive tests by other methods.

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LXXVII

THE BLOOD ALLERGY METHOD IN OTOLARYNGOLOGY

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The following represents a preliminary report of 107 cases of vasomotor rhinitis and associated conditions and precipitin tests on the blood of those patients. The majority had consulted an otolaryngologist for the usual combination of symptoms peculiar to those susceptible to an allergen. A variety of pathological conditions existed in a large number.

The procedure is particularly an advantageous one for the otolaryngologist in that an accurate estimate of the allergenic element can be obtained and treatment undertaken early. The patient may be desensitized to the allergen which produced the vasomotor rhinitis or the allergic status, with its nasal obstruction, sneezing, watery nasal and ocular discharge, together with their prolonged associated chronic states. Nasal polypi may be retarded in growth. Allergic sinusitis, headache both unilateral and bilateral, and occasionally vertigo and eczema may be at least held in check.

It is, of course, understood that accepted treatment for local conditions was carried out during the period of waiting for the return of the findings or during the immunization or desensitization of the patient.

These measures consisted of shrinking sprays plus calcium therapy and at times electrocautery or chemical cautery of the inferior turbinates. The employment of vasoconstricting drugs or combinations of drugs was necessary in many instances.

If polypi were present, they were removed. If x-ray study showed secondary infection of the sinuses in these allergic patients, drainage was established. There was a minimum of operative procedures on the sinuses. Only patients with polypoid changes and pus in the sinuses were operated upon. Three of six patients required maxillary, frontal, or ethmoid sinus surgery. These procedures were followed by desensitization therapy. I doubt that surgery alone would have caused as continued improvement as these three patients obtained.

Desensitization was attempted in such cases as were more severe in type. Avoidance of the allergen in others less severe was undertaken.

Of 15 cases of histamine sensitivity, determined by the method described by Healy,[1] 13 were relieved completely; of these, 7 were of the unilateral headache variety. The remaining 6 were of the vasomotor rhinitis type. All histamine-sensitive patients were over the age of 30 except two. There was, I believe, the most spectacular improvement in the histamine group.

Desensitization in histamine-sensitive patients was done by one of two methods. The first method, when practicable, was by means of intramuscular injections of 1:1,000,000 dilution of histamine phosphate which was given at biweekly intervals starting at 0.5 cc. and increasing the dose by 0.1 cc. until 0.3 cc. was reached. This was continued for 14 or more doses.

The other method of desensitization was oral administration of 1:30,000 dilution of histamine phosphate, 15 drops in water, three times a day after meals, together with nicotinic acid, 25 milligrams, three times a day. The use of nicotinic acid apparently facilitates absorption of the histamine when administered orally.

This oral method required several months as a rule to effect its purpose. No reactions other than local were observed in either method.

Simple questionnaires were sent out one year ago. One hundred seven of those returned showed improvement, and 22, no improvement.

There were eight of the series who for one reason or another did not follow directions or carry out treatment and were not improved. Findings would indicate six of these probably would have had relief, had they done so. Of the two remaining patients, one had an old postoperative sinusitis, having been operated upon eight years previously with resulting unilateral atrophic rhinitis. The other had a similarly very longstanding polypoid degeneration of the posterior inferior turbinal region.

Almost all were patients whose examination and treatment had begun at least two to three years previous to the inquiry so that a fair estimate of response to treatment is indicated.

For many years, many of these patients have had a rather disappointing and disheartening succession of recurrences. To the otolaryngologist they have been a source of feeling of inadequacy in

restoring some of the patients' former physical well-being and general outlook.

A simple office procedure has been found which gives a fair amount of accurate information. It consists merely of the withdrawal of 1 cc. of venous blood and adding 5 cc. of water. The blood is then sent to the laboratory and the allergens are made known directly. Usually the report contains only between one and six allergens. This precipitin test is a definite advance in sensitivity determination, in that it is simple and less time consuming. Consequently, to date over 500 such patients have been under study and will be subject to further report. We cannot claim 100 per cent cure in these cases but a considerable increase in the percentage of relief represents a marked improvement over earlier methods.

There were seven patients in the series who returned for treatment since one year ago and whose conditions may be classified as recurrences. None of these cases was of marked severity and none required protracted treatment, several being intercurrent upper respiratory infections.

I have seen cases of allergy occurring for the first time in the fourth to eighth month of pregnancy. These patients have given no previous history of allergy. We are not prepared now to evaluate these cases, but further study will be done and will be reported subsequently.

Tables follow showing various phases of allergy encountered, and the patient's response to treatment, together with the operative procedures performed.

CONCLUSIONS

1. A method is presented which facilitates arriving at early diagnosis and treatment, as well as being extremely convenient for both patient and physician.

2. Encouraging results to date give expectancy of our being able to lessen the duration and the recurrence of interrelated allergic manifestations.

3. The accuracy of the blood reaction is gratifying, and histamine therapy has definite value.

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TABLE 1

COMPLICATING FACTORS	IMPROVED (72)	UNIMPROVED (9)
Polypi	17	2
Headache, unilateral	9	0
Headache, bilateral	21	1
Eczema	5	2
Asthma	4	1
Sinusitis	6	1
Hives	4	1
Vertigo	2	0
Deafness and tinnitus	4	1

TABLE 2

Total cases	107
Improved with treatment	85
Unimproved with treatment	14
Unimproved without treatment	8
Ages: 50 patients over 35 years of age. Youngest, 11 months; oldest 73 years.	
Duration of symptoms: 2 months to 21 years.	

TABLE 3

ALLERGENS RESPONSIBLE IN IMPROVED CASES

Food	32
Feathers and animal emanations	29
Dust and mold	27
Bacteria	26
Histamine	13
Pollen	10

TABLE 4

ALLERGENS RESPONSIBLE IN 14 UNIMPROVED CASES

Animals and feathers	7
Bacteria	5
Dust and mold	4
Histamine	2
Pollens	1

TABLE 5

OPERATIONS IN IMPROVED CASES

Cautery of inferior turbinates	26
Polypectomy	17
Sinus operative procedures	3
Submucous resection	2

LXXVIII

SUBDURAL EMPYEMA OF FRONTAL SINUS ORIGIN

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Subdural empyema resulting from frontal sinusitis is a common pathological condition that is infrequently recognized clinically. It is rarely discussed in rhinological literature, and merely mentioned in many textbooks. Known by a variety of names including subdural abscess, intra-pia-arachnoid abscess, phlegmon-meningitis, cortical abscess and circumscript meningitis, the condition is more correctly described by the term subdural empyema as pointed out by Kubik and Adams.[1] Subdural pus collections were recognized at least a century ago. Guthrie[2] in 1847 referred to them as a complication of head injuries. An excellent paper by Kubik and Adams in 1943 reviewed the subsequent literature. Hecquet[3] did much to establish subdural empyema as a clinical entity. Writing of middle ear disease, he established the presence of acute or chronic ear infection followed by systemic infection and then rapidly by signs of meningeal irritation, increased intracranial pressure and signs of focal cerebral involvement, indicative of subdural pus. The course of the disease, once overwhelming infection has occurred, is most difficult to control and present-day surgery and chemotherapy have not answered the problem. Yearly, many cases will continue to be seen and newer surgical techniques and chemotherapeusis employed. Meanwhile, much can be done by the general practitioner or specialist called upon to treat infectious processes of the paranasal sinuses and ears. At present one of our most potent weapons in the treatment of subdural empyema is its early recognition. It is to call attention to early recognition of central nervous system involvement as a complication of frontal sinusitis and to emphasize proper therapy that this paper is written.

REPORT OF CASES

CASE 1.—A 36-year-old white soldier was admitted semicomatose to the neurosurgical services of a United States General Hospital in England, November 20, 1944. The accompanying history stated

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that he had suffered from chronic sinusitis for many years and three days previously he had undergone a minor operative procedure to drain the frontal sinuses. He had received adequate doses of sulfadiazine and penicillin for several days prior to surgery and continuously thereafter. On the second postoperative day, there was little purulent drainage from the frontal sinuses and the patient complained of severe frontal headache. The following afternoon weakness of the left side of the body was noted and he was immediately transferred to a neurosurgical center. On examination, the patient was irrational. His oral temperature was 104° F. (40° C.); pulse, 120; respiration, 26; blood pressure, 108/70. The neck was moderately rigid. The pupils were round, regular and equal, and responded to light. The disks were normal in appearance. Tests of extraocular movements were carried out in all directions. A small amount of purulent drainage was present in the nose. There was drooping of the left side of the mouth and speech was incoherent. Weakness of the left arm and leg was present. The deep reflexes on the left were hyperactive and a left-sided Babinski sign was present. The abdominal reflexes were lost on the left. Lumbar puncture was immediately performed. Opalescent fluid under 120 mm. of water pressure was obtained. There were 350 cells per cubic millimeter, all of which were polymorphonuclear leucocytes. Later the spinal fluid culture was reported as negative, the total protein as 40 mg. per 100 cc., and the sugar as 60 mg. per 100 cc. The Pandy reaction was moderately increased. Blood count: red blood cells, 4,500,000; white blood cells, 16,000; hemoglobin 14.5 grams. The urine was normal. X-ray films of the skull revealed densely clouded frontal and ethmoid sinuses without erosion of bone.

The patient was immediately taken to the operating room and a right frontal burr hole was made. The dura appeared reddened and inflamed; the dural vessels, engorged. It was not unusually tense. On opening the dura a large quantity of yellowish-white purulent material welled up into the wound. Despite vigorous irrigation of the subdural space with sodium chloride solution, when a midparietal burr opening was made abundant subdural pus was obtained. A third opening was made in the right postparietal area with similar findings. When irrigation through the three openings obtained no further pus, the subdural space was irrigated with 240,000 units of penicillin in 100 cc. of sodium chloride solution. Two small, soft rubber catheters were placed in each opening and sutured to the skin. The purulent material yielded a pure culture of Streptococcus beta hemolyticus, which was reported as "sensitive to penicillin in

very high dilutions." Following operation, the patient was considerably improved for two days. The temperature ranged between normal and 102° F. (38.9° C.). Penicillin was administered intramuscularly in doses of 20,000 units every four hours. Ten thousand units of penicillin diluted in two cc. were injected in each of the six subdural catheters every four hours. A nasal tube was used for the administration of food and fluids. One gram of sulfadiazine with an equal amount of sodium bicarbonate was administrated every four hours. To facilitate care of the patient, an inlying catheter was inserted into the bladder.

On the third postoperative day, the patient was again lethargic. Very little purulent drainage had occurred through or around the subdural catheters. He was again taken to the operating room and a left frontal burr hole was made under pentothal anesthesia. A moderate amount of subdural pus was encountered. Two additional burr holes were made on the left side, each time pus was encountered. The same procedure was carried out on the right side. The patient's condition was improved following the operation. The following day, he responded to questioning. Treatment was unchanged other than to increase the penicillin given subdurally to 120,000 units every four hours. Nasal feedings were unnecessary after the fourth postoperative day. Subdural penicillin was discontinued after one week and 20,000 units of penicillin, administered intrathecally, daily were substituted for five days. The temperature returned to normal 14 days after the last surgical procedure. Intramuscular penicillin and oral sulfadiazine were continued for an additional week, then discontinued. The patient was evacuated to the United States 67 days after admission with no apparent sequelae except an occasional headache. When the patient was heard of several months later, a generalized convulsion had occurred and he was taking small doses of dilantin daily, apparently with success.

Comment: The early recognition of involvement of the central nervous system, adequate drainage of the subdural space, chemotherapy, and the patient's excellent physical condition and the resistance to the infection brought about slow but eventual recovery. Fortunately, the causative organism was very sensitive to penicillin. As in the case reported by Gross,[4] the patient had been adequately treated by penicillin preoperatively so that the importance of this agent when used postoperatively for irrigation cannot be adequately evaluated.

CASE 2.—R. A. S., a 50-year-old white male was admitted to the University of Virginia Hospital in a semicomatose condition on

May 13, 1946. The history, as related by relatives, was that the patient was in good health until two weeks prior to admission when he began to suffer from left frontal headaches. His physician treated him with nose drops and sedation. Four days prior to admission, he became irrational and his temperature was noticeably elevated. Two days prior to admission there were several right-sided convulsions and he became aphasic. He was said to have had a "stroke."

The patient was a World War I veteran and had mild sinus trouble since 1918. Seven years ago an operation was performed on the frontal sinuses in Washington, D. C. Until the present episode there had never been a severe attack of sinusitis.

On examination, the patient appeared toxic. His nutrition was poor. He was irrational and aphasic. The rectal temperature was 101.4° F. (38.5° C.); pulse, 92; respirations, 22; blood pressure, 108/74. The supra-orbital ridges and the glabella were extremely prominent. The neck was moderately stiff. The eyes moved in all directions equally well. The pupils were round, regular, equal and dilated. They reacted sluggishly to light. The fundi were normal. There was no drainage from the nose or any postnasal drip. There was weakness of the muscles of the right side of the face. All deep reflexes were hyperactive. Positive Oppenheim and Gordon signs were present on the right. The remainder of the physical and neurological examinations was essentially negative although the patient's condition precluded detailed examination. Shortly after admission a right-sided convulsion occurred beginning in the forearm and spreading over the entire right side of the body. The head and eyes were turned to the right. The clinical impression from the history and the neurological findings was "subdural empyema from frontal sinusitis." A lumbar puncture revealed opalescent fluid under 60 mm. water pressure. There were 438 cells per cubic millimeter, 90 per cent of which were polymorphonuclear leucocytes and 10 per cent lymphocytes. The Pandy test was moderately increased and the Ross-Jones positive. Spinal fluid chemistry obtained the following day was: total protein 20, chlorides 685, sugar 35. The spinal fluid culture was negative. There were 11.0 grams of hemoglobin per 100 cc. and 12,000 leucocytes per cubic millimeter of blood.

The report on the x-ray films was: "Views of the skull show a localized overgrowth of very dense bone involving some of the cells of the frontal sinuses as well as adjacent bone. The process has involved the supraorbital ridge on the right with some apparent destruction of this structure. No definite break in the inner contour

of the skull in this area can be seen. Two most likely possibilities are malignant changes in a benign tumor of long standing or of infection secondary to blocking of the ostei of the frontal sinuses." X-ray film of the chest was normal.

On May 14, 1946, a left frontal burr opening was made under sodium pentothal anesthesia. The dura was inflamed; its vessels, engorged but tension was normal. On opening the dura, thick yellow pus welled up in the wound from the subdural space. Burr holes were placed in the midparietal and posterior parietal regions on the left with similar results. The subdural space was then flushed with sodium chloride solution until most of the purulent material was removed. The arachnoid was thickened and opalescent. The brain was depressed two centimeters from the dura over the entire left hemisphere. The subdural space was then irrigated with 200 cc. of warm sodium chloride solution containing 200,000 units of penicillin. Two small soft rubber catheters were placed in the subdural space through each burr hole and sewn to the skin. A similar procedure was carried out on the right side. Here, the dura was less inflamed and the quantity of pus smaller, although it was present over the entire cerebral convexity. The amount of purulent material removed from the subdural space was conservatively estimated as 60-90 cc.

The operation was well tolerated and he was considerably improved immediately thereafter. Postoperative treatment consisted of instillation of 240,000 units of penicillin, diluted to 24 cc., into the subdural space twice daily and the administration of 30,000 units of penicillin intramuscularly every three hours. Sodium sulfadiazine was given intravenously twice daily, in 2.5 gram doses followed by 250 cc. of 1/6 molar sodium lactate solution. Sodium phenobarbital, 0.13 grams every four hours, was used to control convulsions. Culture of the subdural pus revealed type 24 pneumococcus and the patient received 240,000 units of specific pneumococcus antiserum intravenously. Penicillin sensitivity tests were not carried out. Concentrated liquid protein diet was given daily by nasal tube feedings. A transfusion of 500 cc. of citrated blood was given. Although the patient's temperature remained elevated, progressive improvement occurred. On the tenth postoperative day, he was able to carry on an intelligent conversation and to sit up and eat. On May 25, 1946, the patient suddenly developed marked dyspnea and pulmonary edema. The respiratory tract was aspirated and a large quantity of frothy blood-tinged sputum obtained. Coma ensued and despite digitalization, intermittent tracheal aspiration and supportive treat-

ment, he expired on May 27, 1946, 14 days after admission. Permission for autopsy was obtained but due to a technicality, it unfortunately could not be done.

Comment: The presence of focal symptoms for at least three days prior to surgery represented dangerous and unwarranted delay, permitting the onset of a diffuse subdural spread of the infection. Extreme toxicity, the patient's rather poor physical condition probably contributed to myocardial failure and death, despite rigorous treatment.

There are numerous routes by which infection may extend from the frontal sinus to the subdural space. The most obvious one is through the posterior wall of the sinus. The natural ostia of the frontal sinuses may be occluded, as so often occurs in chronic disease leading to pus under pressure. A thrombophlebitis of the diploic veins occurs leading to a localized osteitis and necrosis of the bone. Thrombosis of the dural veins and necrosis then opens the potentially large subdural space. Other routes of extension from the frontal sinus to the subdural space are through retrograde thrombosis of the superior sagittal sinus and the superior cerebral veins or through thrombophlebitis of the mucosal veins of the frontal sinus leading directly to the sagittal sinus without involving the bone or the dura. Turner and Reynolds,[5] Kramer,[6] and Courville and Blomquist[7] have presented schematically the possible routes by which intracranial and extracranial foci may reach the subdural space. Ray and Parsons[8] pointed out that as a source of subdural abscess, the frontal sinus is the most important of all the nasal sinuses. Sphenoid, ethmoid, and maxillary sinusitis are often the source of thrombosis of the venous sinuses, but are rarely the cause of osteomyelitis.[9] The anatomical arrangement of the perforating veins of the frontal sinus and the proximity of the dura undoubtedly contribute greatly to dural perforation and subdural empyema.

The infecting organisms usually are pneumococci, streptococci, and staphylococci, as seen in most intracranial infections arising from the sinuses. The organisms are extremely virulent and this factor contributes greatly to the rapidity with which the infection spreads.

Regarding the symptomatology, usually the patient has had a chronic frontal sinusitis and recently an acute exacerbation. Often, one or more operations have been performed on the sinus and following a relatively minor procedure an acute fulminating infection occurs. Frontal headache is severe and the temperature is elevated

to 103°-104° F. (39.4°-40° C.). Once the central nervous system is involved malaise, stupor, cervical rigidity, visual disturbances and extraocular paralyses are often encountered. A progressive hemiparesis involving the face and the upper extremity more than the remainder of the body occurs due to pressure or thrombosis of the cortical vessels. This hemiparesis should be differentiated from that occurring in the intracapsular lesions where the extremities and the face are usually equally involved. Jacksonian or generalized convulsions occur. So important is the sequence of the frontal sinusitis, abrupt onset of the Jacksonian convulsions, hemiplegia and aphasia (if the major side of the brain is involved) that Courville believes it diagnostic of subdural empyema. There is leucocytosis, the count usually varying between 12,000 and 30,000 per cubic millimeter. The spinal fluid pressure varies between normal and 500-600 mm. of water. Apparently in young individuals where the volume of the potential subdural space is small a few cubic centimeters of pus will cause a marked elevation of intracranial pressure, whereas in the aged the larger subdural space may contain abundant material with little or no rise in pressure. Certainly, the presence of a draining sinus may prevent high intracranial pressures. The spinal fluid is clear to opalescent, the protein increased and the cell count elevated to several hundred, chiefly polymorphonuclear leucocytes. Chlorides and sugar are usually normal which may be of value in differentiating this condition from meningitis. Cultures of the spinal fluid yield no growth of organisms unless the arachnoid barrier has been already penetrated.

Roentgenograms of the skull and sinuses are of little value other than to substantiate a diagnosis of sinusitis. Osteomyelitis is rarely seen and at times the profuse bony proliferation occurring in chronic sinus disease may simulate bone destruction and lead to confusion.

The presence of pus in the subdural space leads in time to an overwhelming infection and death. Exudate may be over but one hemisphere or spread to the opposite side beneath the falx. It is doubtful that increased pressure causes its spread to the opposite hemisphere. In both our cases large quantities of pus were present over both hemispheres without elevation of cerebrospinal fluid pressure above normal. On surgical exposure, the dura is thickened and inflamed and its vessels engorged. Opening the dura results in a gush of purulent material. Once the subdural space is relatively freed of pus by irrigation, the inner layer of dura appears shaggy, the arachnoid thickened and opalescent. Normal cerebral markings may be lost because of pressure flattening the gyri.

The treatment of subdural empyema has always been attended by a high mortality rate. Courville and Blomquist[7] reported 100 per cent mortality, Kubik and Adams[1] 85.5 per cent, Kahn[10] 83 per cent and Ray and Parsons[8] 100 per cent. No one method has been employed which merits evaluation. Initially, the treatment of frontal sinusitis is the problem of the rhinologist and it is his responsibility to recognize its complications. It is generally agreed that the persistence of frontal headache despite all efforts at drainage calls for external drainage of the sinuses. All involved bone should be removed and if the posterior plate is involved, it should be removed and the dura exposed. Adequate drainage, chemotherapy, and the use of specific antisera where feasible, will materially reduce the incidence of subdural empyema. Once intracranial exploration is indicated, valuable time should not be lost in operations on the sinuses, osteomyelitis of the frontal bone, mastoids and so forth.[11] A burr hole should be made just above and posterior to the angle of the brow. Should pus be in the subdural space it will usually well into the wound. Small amounts of pus may conceivably gravitate posteriorly and remain undetected through the frontal opening. Hence, a posterior parietal burr opening should be made. When pus is encountered in the subdural space, multiple burr holes should be made and the subdural space irrigated with warm sodium chloride solution. Small, soft rubber catheters placed in the subdural space may be used for the instillation of penicillin solution several times daily. Their usefulness is only for a few days, after which time they become plugged. Very little purulent drainage occurs around or through the catheters. The postoperative care is arduous and time consuming. The patient's nutrition must be cared for by adequate protein, carbohydrate and vitamin intake, best administered through a nasal tube inserted into the stomach. Pulmonary secretions, so prone to be excessive, are usually well controlled by intermittent postural drainage and aspiration of the pharynx and trachea. Digitalization may be indicated in prolonged infection. An indwelling catheter facilitates nursing care. However, early recognition, prompt drainage, adequate chemotherapy and the patient's own resistance are the primary factors in recovery from this insidious and grave disease.

SUMMARY AND CONCLUSIONS

Subdural empyema is a serious and not uncommon complication of frontal sinusitis. It is a true clinical entity and its diagnosis is not difficult. Personal experience with the two cases and review of the literature are the basis for these conclusions:

1. Patients with acute purulent frontal sinusitis should have adequate drainage of these sinuses.

2. Whenever the patient's symptoms cannot be explained on the basis of a pure sinusitis, intracranial complications should be suspected.

3. The onset of Jacksonian convulsions, hemiplegia or aphasia in the presence of the frontal sinusitis usually indicates subdural empyema.

4. Roentgenograms of the skull and sinuses are of little value other than to establish the presence of sinus infection.

5. The presence of purulent material over both hemispheres is not dependent upon increased intracranial pressure, but probably upon the amount of subdural pus and gravitational factors.

6. Adequate drainage of the subdural space through multiple burr holes and the use of large amounts of sulfonamides and penicillin and appropriate antisera are indicated.

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LXXIX

CLINICAL OBSERVATIONS ON THE DIAGNOSIS AND TREATMENT OF HEADACHE WITH HISTAMINE

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There is no more confusing complaint which the patient brings to his physician than that of headache. The treatment of headache has been so unsatisfactory that many of these patients have learned to shift for themselves and have fallen prey to various types of unscientific treatment.

My observations are based upon the reactions which have occurred in a series of patients with various types of headache. They have not all fallen into the proper "histamine cephalgia" pattern. Histamine was given both as a diagnostic and a therapeutic measure.

The symptom of headache is apparently as old as man and, if we are to conclude from paleopathological findings, the pain and discomfort of headache was just as severe in the primitive races as it is now in modern cultured classes.

Although the old trephining operation for the relief of headache seems a bit drastic, yet it does not compare unfavorably with some of the modern forms of treatment, as for example, the radical exenteration of the sphenoidal sinuses, the removal of the gasserian ganglion, and the removal or lifting of and fixation of the uterus.

Histamine is a secretory stimulant. It is a drug which acts upon the autonomic nervous system, principally affecting secretions and the contractions of involuntary or smooth muscles in the various organs which they stimulate or depress.[1] Histamine stimulates the secretion of gastric, pancreatic, and intestinal juices, contracts the involuntary muscles of the bronchial tubes, causes contractions of the uterus and the intestines, and dilates the capillaries.[1]

Although histamine has previously been considered of no therapeutic value, recently, studies and clinical reports are rapidly demonstrating a very widespread use for this drug.

Recently, Horton[2] in a very scientific and scholarly manner has outlined a definite and rational new type of treatment with hista-

mine for a certain type of headache. Rowntree[3] has defined this complaint as a syndrome regularly recurring with severe and often excruciating paroxysmal unilateral headache of brief duration, coming on during the night, affecting middle-aged and elderly persons. The pain conforms to the distribution of the external carotid artery and is due to vasodilatation secondary to the release of histamine; and it can be produced at will in the subjects of this disease.

Although much research work in the past 25 years has been done on the function and action of histamine in normal human physiology, it is only recently that a practical application has been tried. The exact manner in which the patient secures relief has not been established. Apparently, there is an imbalance, which leaves the patient susceptible to his own defense mechanism. Horton has recently developed a technique of using minutely increasing doses of histamine to desensitize and restore either a temporary or a permanent histamine balance.

Patients suffering from this type of headache have all sought relief elsewhere. They are discouraged, despondent, and skeptical. Although they have already been disappointed by many types of therapy which promised relief, yet they eagerly accept any new type of treatment.

Surprisingly enough, about one half of them are men. They are practically all wage earners and want to work. They are not alcoholics or drug addicts. They are inclined to be of normal weight and practically all wear glasses; they have had them changed at least three times and have had their eyes examined twice in the previous year. They have subnormal blood pressures and low metabolic rates. They all admit feeling well when free of headaches and have no more than the average amount of life's worries.

Seldom does one find even a remnant of a focal infection. All suspicious teeth have been extracted and the tonsils removed. In the older patients, a routine of nasal sinus surgery has been done, and in women, a laparotomy has often been performed. All have had some kind of a general check-up. About 25 per cent have tried the cults and had spinal adjustments. The bowels have been blamed in about 99 per cent of the cases and remain under suspicion (by the patient) in fully 40 per cent.

In the summer, most of these patients wear colored glasses and they believe that they are worse in cold weather. They do not have more than the average amount of colds. Practically all have been

treated for allergic reactions and have been found susceptible to some rare substance.

TABLE I

SYMPTOMS	PERCENTAGE
Headache	50%
Head pains	45
Difficulty in breathing	25
Earache or draining ear	20
Tinnitus	5
Fever	5
Lacrimation	25
Drowsiness	5
Frequent colds	10
Loss of hearing	10
Fatigue	5
Sore throat	15
Sinus infection	35
Dizziness	5
No headache or head pain	5

TABLE II

SEX	PERCENTAGE	AVERAGE AGE
Male	45%	45 Years
Female	55	41 Years

From the previous general description of these patients, it can readily be seen that there is no clear-cut type of headache that one can be certain will respond to histamine treatment. I find it better to explain to the patient that the treatment may not do any good and will certainly not act as a permanent cure; also, that the procedure is both diagnostic and therapeutic and the only way to determine its merit, is to try it. Of course, there is no hazard involved, and although the chances of failure are great, yet emphasis should be placed upon the necessity of completing the treatment on an accurate schedule.

The routine course of treatment usually begins with 0.35 cc. of histamine diphosphate, given subcutaneously, with the daily dosage increased by 0.05 cc. until a maximum of 1 cc. is reached. Following the first injection, there is a reaction around the site of injection, consisting of a slightly raised red area about the size of

a 25-cent piece. The patient is sometimes aware of a slight headache, temporal throbbing and flushing, which last for a few minutes. When relief from the complaint is obtained, it is no effort to have the patient continue on a routine schedule. The injections should continue for about 21 days.

It is advisable for one person to be in charge throughout the entire course of treatment and to maintain complete responsibility. A close study of the immediate reaction in each patient is the best index of how to proceed with the regulation of his dosage. For this reason, the patient should be kept under observation for 30 minutes.

Aside from the physiological reaction, I am convinced that there is also a certain psychological relation between the complaint and the treatment. This makes it difficult to determine accurately the exact immediate effect of the drug upon the symptoms of the patient. Without any type of treatment, these headaches and associated symptoms often occur in cycles, with frequent spontaneous remissions.

The fact that the patient is having treatment for the complaint and that the medication is given by hypodermic injection, no doubt brings about a distinct beneficial reaction, and as the symptoms are so closely related to vasomotor disturbances, it seems reasonable to assume that this soothing effect is a very important factor.

TABLE III

RESULTS	PERCENTAGE
Complete relief	55%
Intermittent relief	35
Slight relief	5
No relief	5

During a course of treatments, some of these "headache patients" came to me with the additional complaint of hay fever and asthma. During the histamine therapy, the asthma improved. The improvement was so striking that they were convinced that the relief from the asthma was directly related to the histamine treatment.

I then found this to be such a routine occurrence that I wrote to Dr. Horton and he confirmed my findings by saying that he, too, had seen the same reaction and was preparing a report upon the subject.

Again, we have here the well-known vasomotor relation to asthma, and it is reasonable to assume that the histamine treatment would

react somewhat in the same manner in the asthmatic patient as in the patient with headache.

It is reasonable to assume that the patient will continue to come to the rhinologist for relief of what he believes to be a sinus type of headache. I have seen many of these patients who should have had histamine as a diagnostic as well as a therapeutic test.

REPORT OF CASES

CASE 1.—The first patient I had in this series was a conspicuous and typical clinical case. Mr. E. H., a 58-year-old man, was referred to me on account of a severe intermittent pain in the right side of his face, extending from his lower jaw to his temple. These attacks had occurred over a period of 22 years. Nothing had given him any relief. His pains were intermittent and would come on at night. His right eye frequently swelled shut and was inflamed. There was continuous lacrimation. His headache extended down over the back of his head and neck. During the previous three months, this patient had three severe attacks of pain, which occurred at night. The duration of the present attack was 42 days.

Fourteen years before, the patient had both legs cut off just above the knees in a train accident, and when I first saw him, I thought he had become addicted to opiates on this account. He advised me that morphine gave him no relief. This patient's response to histamine was immediate and spectacular. He slept continuously for 14 hours and after completion of the course of treatment had no recurrence of his symptoms.

CASE 2.—The following case is of interest because of the fact that Miss E. S. is a graduate nurse, aged 32 years, and has had severe attacks of headache for ten years, which were localized principally in her left temple. She had difficulty in breathing at night. Sharp pain would occasionally radiate to the top of her head, causing her to be sleepless. She was working as a county nurse and was out of doors a great deal of the time. Except for the headaches she had always been in good health. Her continuous contact with doctors had afforded her every therapeutic advantage, but with no relief. Her tonsils had been removed. Her teeth were normal. She had never had any sinus infection, no epistaxis and no ear infections.

For the past six weeks her headache had been so severe that her local physician in a small town about a hundred miles away thought that she might be developing an intracranial lesion and advised her

to see me. Because of the fact that she had access to opiates, my first impression was that she might have become addicted to drugs. She was not of a nervous temperament and following my examination, I was certain of the sincerity of her complaint.

The histamine therapy was explained to her and the treatment was immediately started, which she continued to administer herself. Two weeks later, she returned to report that she was entirely relieved of her headaches except for one light attack, and again two weeks later, she came in with a similar report. She gained a few pounds in weight and her disposition was cheerful. She was sleeping well and her nasal obstruction was entirely gone. In this case treatment was carried out with meticulous precision, and being a nurse she was able to identify more accurately the relation of the drug administration to the relief of her symptoms.

CASE 3.—On the same day, Mrs. B. S., aged 30, came to me with the complaint of pain in back of both eyes, congested nose, and difficulty in breathing which was worse at night. This was of three years' duration and she related that it was similar to hay fever, except that she had it any time of the year. She was interested in relief at this time because of the fact that she was three months' pregnant. She had one other child, a daughter, aged four. During the first pregnancy, she had had no trouble of this kind.

Histamine treatment was started in the usual manner and was carried on cautiously for a few days on account of her pregnancy. Her orbital pain was promptly relieved. She did not return regularly for treatment and, after a few days' lapse, she would again seek relief because of the return of the orbital pain. This intermittent type of treatment was probably caused by the fact that she was somewhat concerned about the effect of histamine upon her early pregnancy. She finally decided that she would wait until she was through her confinement to continue.

Other than the symptoms of head pain and difficulty in breathing, she was a normal healthy woman and had never had a serious illness. So far as I could determine, her pregnancy had no bearing upon her complaint and the histamine gave the same reaction as upon a non-pregnant woman.

CASE 4.—Mr. D. C., aged 32, came in with the complaint of severe headache, congestion, cough, and the history of severe attacks of asthma. For several nights he had been unable to sleep. He had lost weight, looked exhausted, was quite depressed, had no appetite and

was desperate for relief. He was immediately placed in the hospital for complete bed rest and histamine injections were started and administered twice daily. This patient slept throughout the following night, his first night in the hospital. He remained in the hospital for two weeks and had no recurrence of symptoms. Following his hospitalization, he returned to work as a grocery store manager and carried on with the histamine injections.

He was entirely symptom free until 14 months later, when he was exposed to sub-zero weather. In a severe storm he was chilled and suddenly had a mild asthmatic attack. He had head pain and returned to the hospital for histamine injections twice daily. Again he was immediately relieved and slept with comfort. This is a most conspicuous example of the direct effect of histamine on an asthmatic condition. Although his headache was also relieved, to the patient, this was of secondary importance.

CASE 5.—Mrs. E. S., aged 50, had the most interesting history of any of the patients whom I have seen. Without any suggestion from anyone, she found that localized pressure over her right carotid artery would give her prompt and continuous relief as long as this pressure was maintained. She was able to demonstrate this, although she had no idea what she was doing. The occipital pain was so extreme that alcohol injections were contemplated by her physician. She also had a right supraorbital pain, which she thought was caused by a carbuncle which she had had one year before and which I had opened and drained at that time, with complete healing.

The pain was so localized in this area that the patient thought this previous infection had some bearing upon this present complaint. Also, for the first time in her life, although she had grown up in this vicinity, she suddenly had a severe attack of asthma, which almost completely incapacitated her. She made an immediate, favorable response to the histamine injections. Her asthma subsided and her headache totally disappeared. Except for a severe attack of influenza, this patient had an uninterrupted course.

CASE 6.—Mr. J. C. was the only patient in this series whom I was unable to desensitize. He was a 62-year-old farmer and his illness had been erroneously diagnosed as cancer of the lung. He had disposed of his farm and prepared to die. His step-daughter insisted that he come to see me. Upon examination, I found no evidence of any cancer.

He had lost considerable weight, had violent headaches and severe coughing attacks with asthma and bronchiectasis. He was

hospitalized, and although he seemed to respond to the injections in that he quickly was relieved of symptoms, yet he reacted violently to each injection of histamine. He had marked flushing of the face, dizziness, and once he became faint. He had, however, recovered enough to make a motor trip to California with his wife and return. He stated that his headache was much worse while he was in dry country.

A few infected teeth were extracted, which apparently made no great difference. Histamine injections were again used and carried out regularly, without any further relief whatever.

This man had lived on a farm all of his life and had had no pulmonary disturbances until the previous summer, when he purchased a threshing machine and was exposed to grain and wheat dust. Also, he was exposed for several weeks to the fumes from the tractor engine.

I am more inclined to believe that the dust from the threshing machine was the primary etiological factor. Although the man was relieved to learn that he did not have cancer, yet he did not derive much comfort from any of the prescribed therapy.

CASE 7.—J. G., a young man of 19, returned home from an eastern college complaining of a vasomotor headache. I had seen him one year before on account of a deviated septum resulting from a nasal fracture. He had had some nasal and sinus surgery performed in another city but received no relief from his headache. These headaches had been attributed to some sinus infection but, when I saw him the second time while he was visiting his parents, I realized that his symptoms were those of histamine headache.

He was able to place his finger on the exact spot on his temple. His pains were worse when lying down and were also aggravated by an upright position. He was not getting enough sleep. He was a grade A student, had a very nervous temperament, and was small and thin. Hospitalization subsequently convinced me that his complaint was sincere. He had noticed that alcoholic drinks increased the severity of the symptoms. Although he had never received any relief from any type of medication, he promptly responded to the histamine injections. These were carried on after he returned to school.

CASE 8.—Mr. E. K. had confusing symptoms of headache, pain in the right side of his neck, and pain in his head, especially on the right side. X-ray films were made to determine if he had a cervical

rib. In the course of the examination, a pair of infected tonsils were removed. He was only slightly better after this.

While visiting in Kansas City, he called upon me to carry on histamine injections which another physician had previously started which he found gave him complete relief. His neck and head pain had completely disappeared and apparently histamine sensitivity had always been the cause of his major complaint.

SUMMARY

It should be kept in mind that any diagnosis which can only be made and proven by some form of therapy always involves many errors. The patient is always more interested in the relief of his painful symptoms than in the diagnosis of the disease.

It is quite common for some simple type of therapy to so identify and clarify a mass of confusing details that a patient may feel that he has been previously very badly handled.

No disease is very confusing when the underlying pathology is completely understood, but to treat a patient for vague symptoms, such as headache, with its wide variety of causes, often leaves the physician as confused, disappointed and dissatisfied as the patient who is the victim of the complaint. Certainly, it cannot be said that histamine is the antidote for all types of headache, and I believe the treatment of this complex complaint will continue to be about as perplexing as ever.

A few atypical cases will respond in a magic manner, which may lead the physician to believe that he now has the complete answer to this problem. Very soon, however, he will learn that such is not the case; yet this should not discourage him from watching for as many of these patients who fit into this category and who are at least entitled to a therapeutic test.

I believe that the patients with typical histamine cephalgia will continue to be rare, and that the borderline cases will respond in a highly satisfactory manner. These sufferers, as well as the medical profession, are deeply indebted to Dr. Horton for his correlation and vivid presentation of this puzzling complaint.

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LXXX

BRONCHIAL ASPIRATION FOR POSTOPERATIVE ATELECTASIS

A SIMPLIFIED TECHNIQUE

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By progressive simplification, we have evolved a method of bronchial aspiration described below. Its success can be determined by the fact that every one of 13 cases so treated in the past three years showed immediate cure of the atelectasis as demonstrated by clinical signs, x-ray, or both. The procedure is conducted at the bedside with minimal disturbance to the patient. In most cases x-ray films of the chest were taken with a portable apparatus just previous to and immediately following the aspiration. The roentgenological demonstration has been highly dramatic in some cases, especially if judged by the shift of the mediastinum, but the clinical effect based on auscultation and percussion was more so.

In one case there was a remarkable improvement of the breath sounds by auscultation, following a very brief and seemingly too-simple aspiration of a three-day old atelectasis while the x-rays demonstrated no improvement. In spite of this no further treatment was given. The complete loss of signs and symptoms by the next morning confirmed the clinical judgment.

Preoperative care includes morphine for allaying the patient's apprehension, and the tight application of a multi-tailed binder to the abdomen for reducing the patient's fear of bursting his stitches. This is a usual requirement, since most postoperative atelectasis cases follow abdominal surgery. In the opinion of the author, they are always the result of the patient's reluctance to cough because of fear of pain or of harming his incision. The use of atropine preoperatively and the unintentional neglect by the nurse, who does not want to disturb her patient with periodic rotation because he appears to be resting so quietly, contribute considerably to the incidence of the disease but are considered to be only secondary to the patient's reluctance to cough.

Brief application of a 10 per cent cocaine tampon preoperatively to each pyriform sinus by use of laryngeal forceps prevents local

spasm and reduces the tendency to gag. Practiced application of this forcep should cause no unpleasantness to the patient and is usually well tolerated. A portable suction machine is set to, but not beyond, 15 inches of negative pressure. Any bedside lamp supplies the necessary light for the head mirror and a glass of hot water the heat for the laryngeal mirror.

The chief implement is a standard, 20-22 Fr. soft, rubber catheter and wire-guide combination, commonly employed in genitourinary surgery. A slight alteration of the curve of the malleable wire adapts it to laryngeal use. The inside of the catheter is lubricated with mineral oil, or lubricating jelly may be applied to the wire guide in order to facilitate the removal of the wire, following insertion into the trachea.

While an assistant holds the patient's tongue, the larynx is viewed with a laryngeal mirror and the catheter with its wire guide is inserted between the vocal cords into the trachea. The mirror is discarded and the catheter is passed farther into the trachea while it is being slipped off the wire guide. The catheter is rotated clockwise for insertion into the right stem bronchus, or counter-clockwise for insertion into the left stem bronchus. The suction machine is attached and negative pressure is applied while the catheter is slid repeatedly up and down for approximately one to two inches. Secretion is seen and heard in its passage through the catheter to the suction machine. During suction, the patient shows a violent tendency to cough, but if properly prepared in advance with morphine and with a simple explanation of what is expected of him, he can be persuaded not to react violently and not to grasp the catheter with his hand. Forceful holding of the patient's hand is occasionally required.

CONCLUSIONS

1. A simplified bedside technique for passage of a soft rubber catheter in postoperative atelectasis is presented.

2. Indirect visualization permits prompt and smooth passage of the catheter into the bronchial tree.

3. It requires no specialized technique other than the use of the laryngeal mirror. The preoperative laryngeal application of cocaine may be omitted if desired.

4. The momentary coughing and disturbance produced by the presence of the catheter after its passage into the tracheal tree

is brief and without danger. It compares favorably with more extensive procedures. The technique has been highly satisfactory to the surgical and medical staffs at Oliver General Hospital.

5. Results have been 100 per cent effective, without complications, and usually immediate. Early in the series, one additional aspiration was done in a case in which the diagnosis was not definite. At that time, there was a difference of opinion on the part of the various consultants as to the differential diagnosis between patchy atelectasis or broncho-pneumonia. This illness progressed to a typical broncho-pneumonia. In retrospect, therefore, the infection was considered to have been pre-existent and not a complication of the manipulation. Since then, all cases have been carefully selected on the basis of a positive diagnosis of atelectasis and no such sequela or complication has been noted at any time. This one case is not included in the group of 13 presented.

6. A total of 14 postoperative atelectasis cases have been treated at Oliver General Hospital during the past three years. A bronchoscopy was performed on the first patient but all of the subsequent 13 patients were treated with the soft rubber catheter technique.

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LXXXI

THE VASCULAR DYNAMICS OF THE COMMON COLD AND ALLERGIC RHINITIS

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The search for the cause of the common cold has been marked by so many failures, it has become obvious that instead of a frontal attack on the bacteriologic aspects an indirect approach through the physiologic changes could lead to fruitful therapeutic results.

An investigation was therefore undertaken to determine the physiologic factors in the vascular dynamics of the common cold. It was important to know what led to the vascular relaxation causing congestion of the nasal mucosa, what influenced the cell permeability with the transudation of serous fluid and the increased secretion of the mucous glands, and the factors underlying the lassitude and the susceptibility to secondary infections so frequent with the common cold. In considering the dynamics of vascular relaxation our attention is focused on the smooth muscle of the vascular tree. In this we must explore the physiology of muscle contraction which gives vasoconstriction as well as the factors in vasodilatation. In understanding muscle contraction we face a complex of reactions which, if we follow them carefully, opens up the field of nutrition as well as the chemistry of the neuromuscular mechanism. In the latter we have the macroscopic sympatho-adrenal medullary system with its chemical liberation of adrenin and sympathin as well as the microscopic motor end plate system which can be considered as an endocrine organ as well because of its production of acetyl choline. Both of these systems are balanced against each other so that while adrenin or sympathin will cause contraction, acetyl choline will cause relaxation and vice versa. To maintain this balance we have several enzyme systems; thus adrenin will be destroyed by an amine oxidase which is found in the blood and in many tissues, while acetyl choline is destroyed by a choline esterase.

Thus we begin to see that maintaining vascular dynamics is a fairly complicated task. When we want to maintain vasoconstriction we can do so by inhibiting the amine oxidase. This is accomplished in various ways. Ephedrine, because it is acted on by the

same enzyme, tends to prevent exhaustion of adrenalin. The principle of its action is called "substrate competition."

When amine oxidase is in contact with adrenalin alone, it destroys it at a certain rate; if ephedrine is present simultaneously, it engages the activity of some of the enzyme which, thus preoccupied, cannot act on adrenalin which is therefore decomposed more slowly. Ephedrine thus tends to stabilize adrenalin liberated at sympathetic endings and so makes it more susceptible to collection and quantitative determination.

In experiments on the blood vessels of the rabbit's ear, the addition of ephedrine to the perfusing fluid increases the resting rate of formation of adrenalin. On stimulating the peripheral end of the cervical sympathetic system the rate of adrenalin formation is normally increased; this increase is much greater if the experiment is repeated in the presence of ephedrine. Gaddum and Kwiatkowski[2] also showed that adrenalin produces a more intense vasoconstriction in the presence of ephedrine; potentially the same effect can be produced by ephedrine on the constrictor response to sympathetic stimulation.

Thus the balancing of the enzymes controlling the destruction of adrenin is a controlling factor in vasoconstriction. On the other hand vasodilatation is also an active process and the result of chemical changes and enzymatic balance in the same manner as vasoconstriction. Here we must consider whether nasal congestion is due to the inhibition of choline esterase with overaction of acetyl choline or to the loss of constrictor tone because of adrenin insufficiency.

In view of the fact that ephedrine overcomes the nasal congestion we are led to believe that adrenin insufficiency is behind the loss of constrictor tone and that the ephedrine is serving as an adrenin-sparing mechanism. This was still further supported by the fact that vitamin C, which, through its reducing properties, has a sparing action on both adrenin and ephedrine, enhances the action of ephedrine and adrenalin in overcoming nasal congestion clinically. Experimentally this action was graphically demonstrated by observing microscopically the relaxation, brought about by adrenalin ascorbate and ephedrine ascorbate, of bronchiolar contraction due to histamine. Adrenalin ascorbate was fully twice as active as adrenalin chloride.

It is interesting to note that of the many sympathomimetics that have been synthesized and have gained application in medical

use none are as free from untoward side-effects as ephedrine. The occurrence of ephedrine in nature probably explains its capacity for substrate substitution for adrenin in the body, whereas the synthetic preparations may not be able to function in that capacity at all but may have a direct action common to amines and similar in response to ammonia. It has been a relatively frequent occurrence to observe prolonged nasal congestion after continued use of privine. This may be due to its failure to react with amine oxidase and its adrenin-sparing properties.

A direct influence on the sympatho-medullary system is also easily attained through medication of the sphenopalatine ganglion.

The mechanism of the actual muscle contraction that gives vasoconstriction is intimately tied up with a series of chemical reactions involving the action of the coenzymes of the vitamin B complex. Through the intermediation of these enzymes in cell respiration, energy is obtained from ingested carbohydrates. An imbalance between the amount of carbohydrate and available B complex coenzyme leads to accumulation of the fatigue-producing pyruvic acid. This may also explain the tendency for increased susceptibility to colds following heavy carbohydrate indulgence. It is therefore important to study closely the chemistry of muscle contraction. Through it we simultaneously get a glimpse at the relationship of the nerve impulse to the actual end effect. This has been described in a previous paper.[9] It was pointed out that the coenzymes of the B complex in conjunction with the adenylic nucleotide controls muscle contraction and through it muscle tone.

Still another factor is involved in muscle metabolism and vasoconstriction and that is the inorganic ion influence and electrolyte balance. Membrane permeability is perhaps the most disturbing element of the common cold and nasal allergy. The profuseness of nasal discharge is part of capillary leakage.

Capillary permeability is perhaps the greatest factor in the vascular dynamics of the common cold. There is diffusion through the endothelial membrane of fluid in bulk without any evidence of a separation of solutes from solvent. This kind of selectivity is quite comparable to that obtained with inert membranes whose pore size permits the passage of molecules up to the dimensions of the larger sugars and some proteins. Retention of the colloidal components of the blood and serum proteins create Donnan equilibria effects and produce an effective source of osmotic pressure on one side of the membrane. However, the structural and functional efficiency of the

barrier is altered by minute changes in the chemical make-up of the fluids on either side of the membrane. These disturbances allow varying amounts of colloid to pass through the endothelial wall, disturbing the colloid osmotic pressure relation and by altering the porosity of the membrane may enormously increase the loss of fluid through it.

Zweifach,[12] in his excellent studies on capillary vessels, showed that the hemodynamics of different capillary circulations introduce different mechanisms of fluid exchange. Single capillary vessels produce a different effect than those where the flow is through a larger number of subsidiary capillaries. A similar situation exists in the nasal mucosa and congestion or clearness may depend on the direction of circulation through either the larger single capillary channels or distribution through a larger number of subsidiary capillaries.

It is interesting to correlate Zweifach's conception with Krogh's[6] findings regarding the site of action of adrenalin. While the vasoconstrictor effect of adrenalin is commonly taken for granted, still Krogh found that the capillaries are refractory toward adrenalin though the larger arterial branches contract readily. He observed that, when small drops of 0.1 per cent adrenalin are placed on the skin or web of the brown frog over an arteriole, it shows no constrictor effect. By following up the artery putting drop after drop over its course, a point is finally reached where the constrictor reaction arises. When the drops are placed a short distance apart and half a minute or more allowed to elapse between the single tests, it is often observed that the artery begins to contract at a certain distance proximally to the last drop and the contraction spreads slowly in a proximal direction while the artery just below the drop remains open. In this light we can weigh the observations of Hartman, Evans and Walker,[4] who found that in muscle capillaries of cats and rabbits adrenalin in small doses causes dilatation and opening up of muscle capillaries with increase in flow. Larger doses, while dilating capillaries, constrict the arterioles.

This opens up the speculation that adrenalin exhaustion with a low level of circulating adrenalin may be responsible for nasal congestion through active dilatation of the capillaries rather than the direct action of the vasodilator apparatus associated with stimulation of the acetyl choline mechanism. However, the maintenance of a normal adrenalin balance and the use of adrenalin-sparing substances such as ephedrine and vitamin C would seem to have a definite rationale.

The question of electrolyte balance is our remaining factor in membrane permeability. Here we find the pH playing a close relationship to calcium, sodium and potassium. While Krogh ascribed capillary permeability to the endothelial cell, it is evident that many substances to which living cells are impermeable readily pass through the capillary wall, indicating that the intercellular structure plays an important role in capillary permeability. The intercellular cement had been suspected of playing a role in capillary permeability as far back as 1897 by Ringer, by Herbst[5] in 1900 and Overton[7] in 1904. They stressed the existence of a cohesive material consisting of a reversible calcium salt of a weak acid for binding cells together. They pointed out that as a consequence the physical state of cellular membranes could be varied by changing the pH and calcium content of the medium. It was not surprising therefore to find that variations in the permeability of the blood capillaries of the frog could be readily induced by subjecting the vessels to conditions which Ringer, Herbst and Overton found to affect the intercellular cement.

Direct observations were made by Chambers and Zweifach[1] on the capillary circulation in the mesentery of the frog while perfusing the animal with ash-free gelatin mixtures, the pH and calcium content of which were varied. The indications were that the permeability of the endothelial membrane may be explained without taking into account the permeability of the individual cells. The endothelial cells themselves may be selectively permeable, but the porosity of the cement is of such a magnitude that movements through it swamp out any selective effects of the cellular components. Today, of course, we know that the intercellular cement is subject to the vitamin C level and in earlier papers[8, 9] I pointed out that the formation of a calcium, vitamin C proteinate is the normal complex of serum calcium. It was on that basis that I recommended calcium ascorbate as the ideal form of calcium therapy.

In their experiment Chambers and Zweifach showed that when the perfusate contained double the normal amount of calcium, especially when it was acidified to pH 6.8, the deposition of cement on the inner surface of the capillary markedly increased the resistance encountered by the circulating fluid. Perfusion with calcium-free solutions caused the capillary wall to become excessively leaky. A progressive washing away of the cement occurred, especially in the more acid pH ranges. Stasis and edema appeared extremely early in the acid pH ranges. The effects obtained in the absence of calcium were completely reversed by changing to the calcium perfusate. An increase in the acidity of the normal perfusate to pH 6.6-6.8 was

followed by pronounced leakiness. In the alkaline pH ranges 7.8-8.0 the cement appeared to be increasingly stabilized and edema was absent for over two hours. With increased alkalinity and acidity respectively of the medium the permeability of the capillary wall reached comparatively constant values and the effects predetermined.

From these results it is apparent that the alkaline calcium and sodium ions play an important role in vitamin C usage. When using ascorbic acid in large dosage, it is obvious that the sodium ascorbate or the calcium ascorbate is more important in the control of membrane permeability than the free acid.

Increased acidity increased the ionization of the cement and thereby enhanced its dissipation. An important role of the endothelial cell would appear to be the continual secretion of an intercellular cement, the chemical stability of which controls the permeability of the blood capillary. The intercellular cement comprises the actual filter and has deposited on it a layer of protein from the blood. In an earlier paper on the physico-chemical properties of calcium ascorbate,[9] I pointed out the tendency for vitamin C to form serum protein complexes. This plays an important role in the porosity of the capillary wall to the extent of preventing the colloidal constituents of the blood from leaking through. Thus the role of calcium, sodium and potassium ions is a vital role in membrane permeability.

While all these chemical and physical factors have been considered from the angle of membrane permeability and muscle tone in the vascular dynamics of the common cold and nasal allergy, we still have two further aspects to consider, the mechanics of inflammation and the mechanics of allergy. Both may be said to have a common relationship in that histamine is liberated in both instances, and in the extremes of both conditions shock may supervene. Capillary permeability is increased in both conditions, with formed blood elements escaping by diapedisis and direct penetration of the capillary wall most pronounced in inflammatory reaction. Since the intercellular cementum is the target for the break-through, we must consider histamine to be uniquely capable of disrupting the calcium protein ascorbate complex.

Clinically, I have been able to show that high dosage of vitamin C, particularly in the form of the calcium or sodium salt, was effective in controlling both the inflammation of the common cold and nasal allergy. To demonstrate the difference between ascorbic acid and sodium ascorbate, a series of nasal allergy cases were treated with sodium ascorbate in high dosage. Those cases particularly were

selected where the results of ascorbic acid were not as favorable as was to be expected, although by and large the majority of allergic cases responded well to a high dosage of ascorbic acid. In some of the cases, the sodium ascorbate was completely successful where only moderate relief was experienced with the ascorbic acid. In these instances it would appear that the sodium ion caused an increased diuretic effect that diminished the transudation of fluids from the nasal membrane. Also the role of pH, particularly maintenance on the alkaline side, is apparently more important than we have hitherto believed.

SUMMARY

1. The vascular dynamics of the common cold and nasal allergy may be attacked through the physiologic disturbances in muscle metabolism, particularly that of adenylic acid and the coenzymes of the vitamin B complex as well as in muscle innervation by the sympathoadrenal mechanism through adrenin sparing by ephedrine.

2. Capillary permeability responsible for the transudation of fluids is primarily due to disturbances in the intercellular cementum and is in direct relationship with the calcium level and pH of the circulating fluids.

3. A high calcium level and an alkaline pH increase the resistance to capillary leakage.

4. The indications for treatment based on physiological and clinical experimentation point to the use of ephedrine for adrenin sparing, vitamin C for intercellular cementum preferably as the ephedrine ascorbate, the administration of vitamin C as the calcium and sodium salts for alkalinity.

32 EAST 67TH STREET.

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LXXXII

SINUS THERAPY BY THE USE OF VOLATILE INHALANTS

PRELIMINARY REPORT

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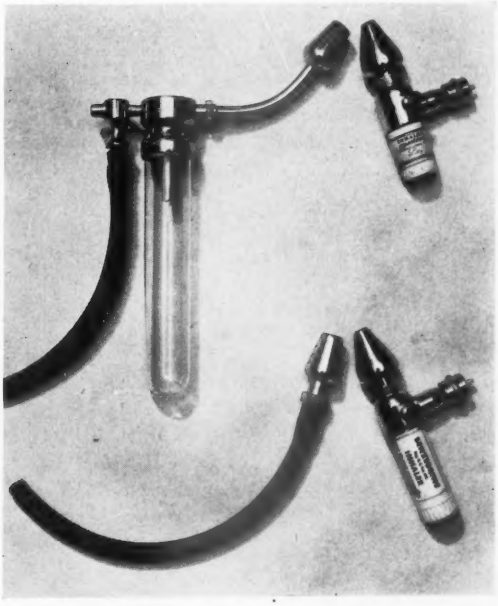
The principle of introducing liquids into the nasal sinuses by means of the displacement method has been well established through the basic work of Proetz.[1] The same author, in a recent article, has described a method for introducing gases into the sinuses.[2] In his article, Proetz calls attention to the present availability of powerful vasoconstrictors in the form of vapor inhalers, such as 2-aminoheptane (Tuamine-Lilly). Other volatile vasoconstrictors are also available, for example, Amphetamine, (Benzedrine-Smith, Kline, & French) and Phenylpropylmethylamine (Vonedrine-Merrell).

I have devised an arrangement for the use of volatile vasoconstrictors which consists of an ordinary nasal sinus suction cleanser and a specially constructed suction inhaler. The latter is a small metal cylinder to which can be screwed an ordinary commercial inhaler, after first removing its cap. The threads of the metal cylinder are made in three sizes, since the screw threads of the chief commercial inhalers vary. On one side of the metal cylinder are a finger suction-release opening and a valve which is regulated to release the suction automatically when it reaches 180 mm. Hg. A detachable nose piece can be removed for sterilization.

The procedure in treating the patient requires the preliminary use of a mildly anesthetic astringent spray, followed, if secretion is present in the nasal cavity, by aspiration with a thin suction tip.

With suction pump running, place both nosepieces securely into both nostrils. Place the left thumb on the control opening of the suction cleanser and the right thumb on the opening of the inhaler. The patient says "K K K," thus closing the soft palate. Suction is created and is automatically regulated to 180 mm. (Proetz) by the relief valve. Air relieving the resulting vacuum as the valve opens travels through the inhaler into the right nostril through the nosepiece and is withdrawn through the left nostril. When the vacuum



has been built up to maximum, remove the right thumb from the opening, thereby releasing the vacuum and filling the sinuses with vapor. The same procedure is repeated about five times. A greater number of applications may cause vertigo. A suction tube and nosepiece shown in the illustration may be used instead of the sinus cleanser. This enables the patient himself to hold the nosepiece, giving the operator a free hand. I employ this procedure except when a large amount of secretion is present, in which case I use the sinus cleanser.

Thanks are due to Mr. Fred Sorenson of the C. M. Sorenson Company for his valuable cooperation in making up the apparatus.

100 EAST 74TH STREET.

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Clinical Notes

LXXXIII

ADAMANTINOMA OF THE MAXILLARY SINUS

REPORT OF TWO CASES

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Two cases of adamantinoma of the maxillary sinuses are reported from the Otolaryngological Services of the Presbyterian and the Research and Educational Hospitals, Chicago, Illinois. One presents an atypical and the other a typical microscopic picture of this tumor.

In the articles used as reference studies, only 12 of 77 maxillary adamantinomas definitely involved the maxillary sinus and two had questionable association with it. These articles comprised the literature of the past ten years. Authors had definitely to mention the site of discovery as one or other maxillary sinus before we classified the growth as an antral tumor.

Upon the basis of these two cases and the perusal of the literature it was decided to review thoughts regarding the growth as well as reiterate previously stated methods of treatment of this tumor when it involved the maxilla or its accessory sinus.

CASE 1. (Central Free Dispensary No. G-33981). The patient, a 67-year-old white male, entered the clinic on February 25, 1941, with a chronic cough. Examination revealed a high septal deviation and darkening of the maxillary sinuses to transillumination. X-ray films (Fig. 1) of the sinuses revealed "marked clouding of both antra" with the other sinuses clear. Bronchoscopic aspiration of thick tenacious secretion resulted in marked improvement of his cough. Five subsequent aspirations between this date and July 14, 1942, were performed with abatement of this symptom.

After nearly three years the patient again returned to the clinic with the complaint of difficulty in breathing through the left nostril.

Fig. 1.—J. H. This roentgenogram taken February 25, 1941, shows clouding of both maxillary antra. Area outlined by the arrow appears throughout all the roentgenograms. The medial border of this area shows small niche-like points and could be interpreted as air remaining in the sinus or the early site of origin of the tumor.

It was noted on nasal examination that the left inferior turbinate was swollen and pressed against the septum. The maxillary sinuses were dark on transillumination and a neoplasm was suspected. The sinuses were again x-rayed (Fig. 2) and the report of March 16, 1945, reads, "some clouding of the left antrum and ethmoid sinuses with other sinuses clear."

Biopsies of specimens taken from the nose by biting forceps on March 21, April 9, and October 17, 1945, were successively reported by the pathologist as "subacute inflammation", "granuloma (character not apparent)", and "chronic inflammatory change in mucous membrane".

Fig. 2.—J. H. This roentgenogram taken March 16, 1945, shows dense clouding of the left antrum and obliteration of the nasal landmarks and air spaces on the left. Note the niche-like erosions indicated by the arrows pointing to the left infraorbital plate and an increased thickness and density of the medial trabecula outlined in Fig. 1. The nasal septum deviates to the right and may be explained by the history of trauma.

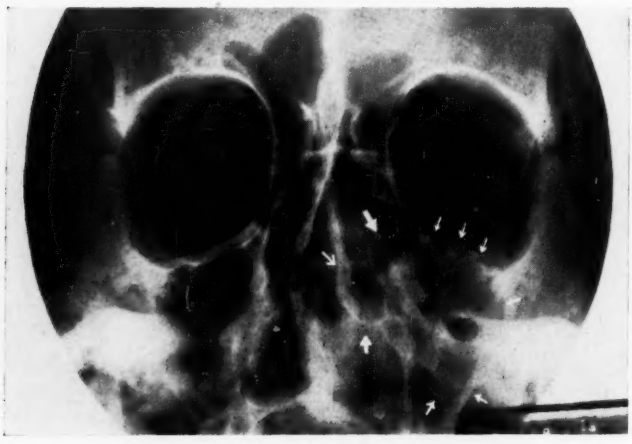

Fig. 3.—J. H. This roentgenogram taken December 13, 1945, shows that erosion of the left infraorbital plate is complete; the antrum is filled by a mass which has begun to involve the antral floor. There are areas indicated by arrows which appear cystic in character. There is almost complete obliteration of the normal landmarks within the nose indicative of a destructive tumor of the left antrum.

On December 13, 1945, the patient was again seen. At that time the impression of a carcinoma of the left antrum was recorded. X-ray films were again taken (Fig. 3) and showed: "marked clouding of the left antrum with destruction of the upper rim of the antrum and the floor of the orbit, suggesting a tumor of the antrum."

On January 10, 1946, a Caldwell-Luc exposure of the left antrum was performed. A bluish, cystic mass was seen on removing the remainder of the partly eroded canine fossa. Bleeding was not excessive and the sinus was cleaned out thoroughly. A window was made beneath the inferior turbinate into the nasal cavity and the patency of the left nasal passage was apparently restored. The patient was discharged in three days without incident.

The pathological report was: the tumor varies in character from place to place and is composed primarily of immature cells resembling those of embryonic mesenchyme. These cells make up the bulk of the stroma and also form cystic structures. In these multiple cysts which comprise a major part of the tumor there are two types of tissue. One is a loose-textured, vascularized and mucinous connective tissue, while the other is acellular and composed exclusively of mucinous material. Mitotic figures are rare. In some areas, where the stroma is dense, the tumor resembles mixed tumors of the parotid; in others it resembles an adamantinoma but is certainly not an ordinary type of carcinoma. Diagnosis: Adamantinoma(?). Photomicrographs of the tissue are shown in Figures 4, 5 and 6 (Presbyterian Hospital 58207; Army Institute of Pathology Accession No. 167844). This pathologic diagnosis was confirmed by three eastern and two Chicago pathologists.

Following this diagnosis surgery was not considered because of the advanced age of the patient. The Tumor Clinic considered the tumor comparatively benign and the policy of watchful waiting was adopted with frequent observation of the patient.

The antrum window was maintained by frequent sinus irrigation. An x-ray film was taken on February 7, 1946 (Fig. 7) and showed, "clouding of the left antrum and ethmoid sinuses with destruction of the medial wall of the antrum and the superior wall, extending into the left orbit." There was no marked intranasal evidence of recurrence of the tumor or extension into the nearby structures.

On April 11, 1946, the patient entered the clinic complaining of pain beneath the orbit, over the left maxillary sinus and at the inner canthus of the left eye. This pain grew worse with digital pressure

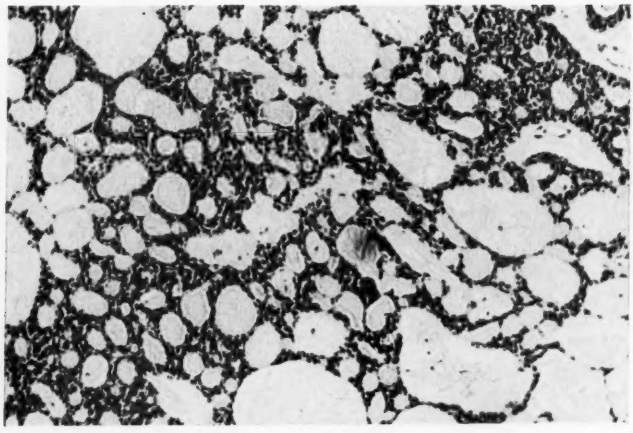

Fig. 4.—J. H. Photomicrograph of section of tissue removed from left antrum. This photograph shows a field where immature cuboidal cells form cysts of varying size. Between the cysts there is loose-textured, vascularized, mucinous connective tissue and an almost acellular tissue composed almost exclusively of mucinous material. (January 10, 1946.) x60.

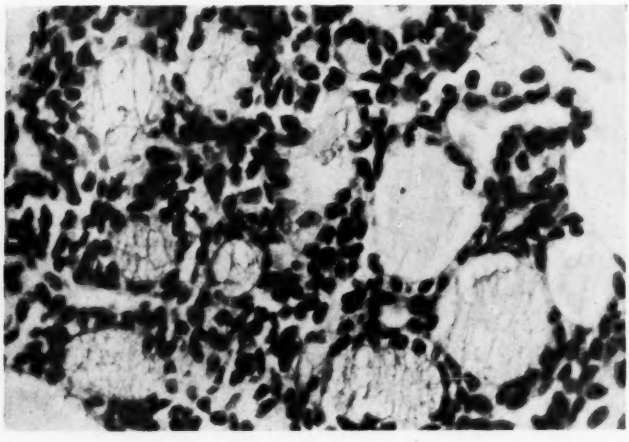

Fig. 5.—J. H. Photomicrograph at a higher magnification of an area shown in Fig. 4. x265.

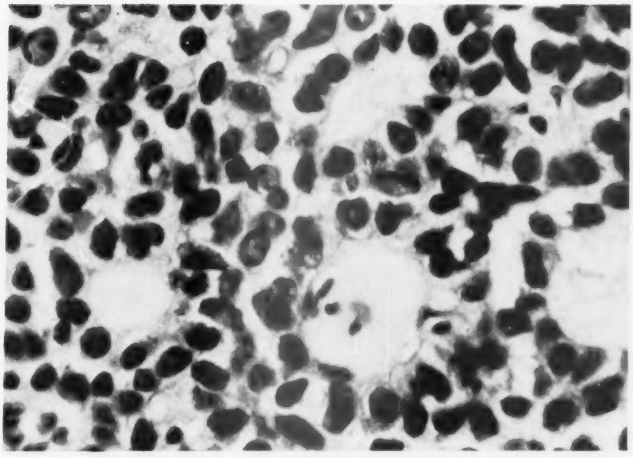

Fig. 6.—J. H. Photomicrograph illustrating the embryonic type of mesenchymal cell which lines many small cysts. There is no sharp differentiation between cells which line the cysts and those which lie in the stroma between cysts. x445.

and a lancinating pain radiated over the edentulous left upper gum margins. Antral irrigation produced shreds of pus and ropy sanguineo-purulent material for the first time since the previous operation. The patient's cough had returned.

Roentgenograms of the skull and the chest were negative but those of the sinuses (Fig. 8) taken on April 12, 1946, showed a definite central tumor mass on frontal view. The Tumor Clinic urged us to undertake a left radical antrotomy with endoral removal of the hard palate, the alveolar ridge and the lateral wall of the nose together with the turbinates and such portions of the tumor as were accessible. All were agreed that hemisection of the maxilla would be too radical, but accessibility led us to undertake an external approach. No cervical lymphadenopathy had ever been noted.

On April 24, 1946, the operation was performed with nitrous oxide, ethylene and avertin as the anesthetic agents. Ligation of the left external carotid artery preceded a Ferris Smith type of approach to the antrum. The incision extended from the supraorbital ridge around the inner canthus almost to the outer canthus of the left eye.

Fig. 7.—J. H. Roentgenogram (basomental view) taken March 7, 1946, one month after the left Caldwell-Luc exposure and curettage of antrum reveals that the ethmoid labyrinth is uniformly dense and the lamina papyracea is absent although it had previously appeared on x-ray films. These findings would indicate inadequate removal of the neoplastic tissue.

Upon elevation of the periosteum from the canine fossa and the left nasal bone, one noted a tumor extending through their friable and necrotic remnants. The opening was enlarged and a whitish, cystic tumor, well circumscribed and encapsulated by mucosa, was seen. The tumor resembled a large gooseberry and completely filled the left antrum. It separated easily from the septum along with the lateral wall of the nose.

The infraorbital plate and the lacrimal bone were removed on the left without entering the periorbital fat or disturbing the fascial slings of the orbit itself. The ethmoid cells were exenterated and a finger-like projection of the tumor was followed into the left frontal sinus. The anterior wall and the mucosa of this sinus were completely removed. The alveolar ridge was taken for biopsy along its length and the hard palate was removed but an intact buccal mucosa was left behind.

The mucosa of the maxillary sinus was removed with all suspicious areas of bone erosion. Exenteration was limited superiorly by the cribriform plate, posteriorly by the sphenoid, inferiorly by the

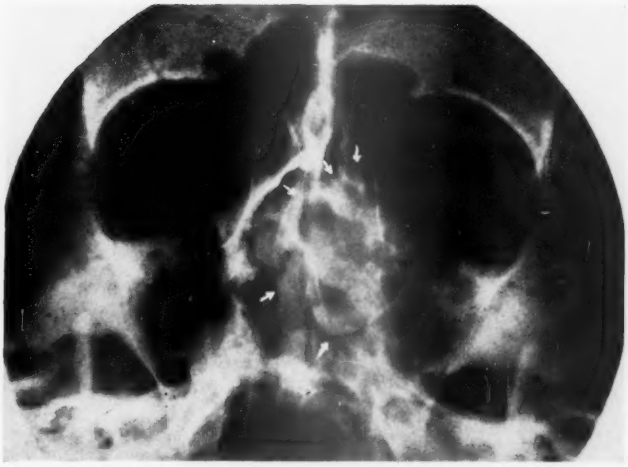

Fig. 8.—J. H. Roentgenogram (basomental view) taken April 12, 1946, reveals a definite neoplastic mass which has progressed through the nasal septum to impinge on the right lateral nasal wall. It is almost uniformly dense and circumscribed. It lacks the cystic character evident in previous x-ray films. The left antrum appears to be less dense than the tumor mass. A suspicious projection from the tumor seems to involve the nasofrontal duct and inferomedial margin of the left frontal sinus. This roentgenogram led to a radical left antro-fronto-ethmoidectomy and enucleation of the entire central mass with removal of the necrotic left infraorbital plate.

buccal mucosa and the alveolar ridge and laterally by the pterygomaxillary fossa and the lateral wall of the antrum.

The incisions were closed with interrupted subcutaneous sutures of chromic catgut and black Dermalon 5-0 interrupted mattress sutures were used for the skin. The lacrimal sac and the inner canthus of the left eye were approximated firmly to muscle and skin in approximately normal position prior to skin closure. The cavity was packed with gauze.

Penicillin was administered in doses of 20,000 units every three hours as a prophylactic measure. The patient ate a regular diet on the second postoperative day and was discharged on the sixth without incident.

Specimens of tissue sent to the pathology laboratory for study were again reported as adamantinoma. The tumor's invasive char-

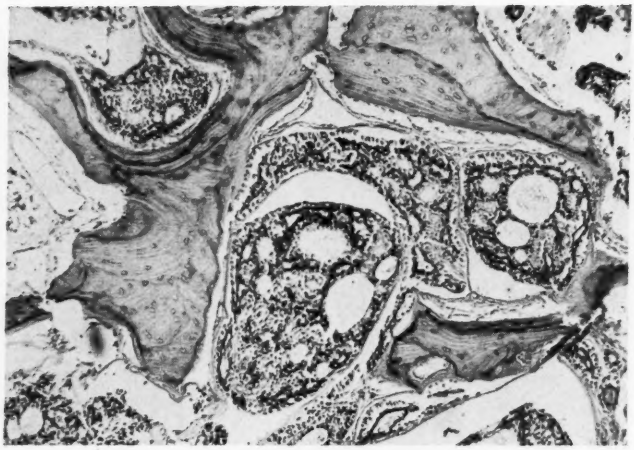

Fig. 9.—J. H. Photomicrograph showing osseous structure of the left infraorbital plate. The cancellous spaces are filled with masses of invading neoplastic cells. Cell types similar to those shown in other photomicrographs are noted as are the cysts enclosing mucinous material. There is evidence of resorption and new formation of bone adjacent to groups of neoplastic cells. (April 24, 1946) x60.

acter is shown in Figure 9, a photomicrograph of portions from the left infraorbital plate. Specimens from the alveolar ridge interestingly revealed no evidence of tumor tissue.

The patient was seen on May 14, 1946, at which time no x-ray evidence of further tumor growth was noted. He has a diplopia in all quadrants but is not bothered by this as his central vision allows reading without discomfort. He complains only of slight tearing from his left eye and carries on his normal daily tasks.

CASE 2. (Research and Educational Hospital, OPD No. 311400). A white female, aged 45, first presented herself to the Out-Patient Clinics on October 30, 1945, complaining of aching pain in the right side of her face radiating to the occiput, the right eye and the ear, which had been growing progressively worse for the past three years. On occasions the pain would last several hours. Examinations were negative except for an area of irritation from dental plates which was noted on the right upper gum margin. The patient was referred to the Ear, Nose and Throat Service.

Fig. 10.—I. M. Roentgenogram taken November 20, 1945, shows bone destruction involving right upper alveolar ridge and the floor of the right antrum.

The patient was seen by the latter service on November 5, 1945, and a "swelling" of the upper right alveolar ridge was noted, with tentative diagnoses recorded of trigeminal neuralgia and pathological changes of the bone, such as osteitis fibrosa cystica.

Roentgenograms (Fig. 10) were taken on November 20, 1945, which revealed bone destruction involving the right upper alveolar ridge and the floor of the right antrum.

On December 3, 1945, the patient was admitted to the hospital for biopsy of the right upper alveolar ridge.

The pathological report was: interlamellar spaces of bone are widened and reveal infiltrating masses of epithelial strands, some of which are solid, while others present central lumina lined by tall, orderly cells peripherally but are multi-layered. These are associated with a moderate amount of fibrillar connective tissue. Diagnosis: Adamantinoma (Fig. 11).

Fig. 11.—I. M. Photomicrograph showing tissue taken on December 3, 1945 from the right alveolar ridge. The irregular lamellae show osseous resorption with some new bone formation and invading masses of neoplastic cells. Some epithelial strands are solid and others present central lumina. These are lined by fairly tall, orderly cells peripherally but are multilayered strands and associated with a moderate amount of fibrillar connective tissue. x42.

Further questioning of the patient revealed that she had a long dental history with only six lower molars remaining of her secondary teeth—described as nothing but "pegs and decayed roots."

On January 5, 1946, the patient's right external carotid was ligated and the right maxilla resected. The pathologist again reported typical adamantinoma scattered throughout the bone and up to the mucosa of the bony tissue of the antrum, alveolar ridge and maxilla. The patient was discharged without incident on the thirteenth postoperative day.

A false denture was prepared following healing of the wound. Specimens taken from the wound site on March 11, 1946, revealed no evidence of tumor tissue. Some foreign body giant cells were identified.

The patient was seen on April 8, 1946, and referred to the Neurological Department for paresthesia of the fingers and slight paralysis of the left arm and leg. The neurological consultant's

report was "evidence of left-sided pyramidal tract involvement. There may be metastases of primary lesion for which she will be observed in neurology clinic." She continues to return to the Ear, Nose and Throat Clinic at fixed intervals for observation. No definite recurrence had been noted by May 10, 1946. No cervical lymphadenopathy was noted.

REVIEW OF THE LITERATURE

Boyd[1] defines adamantinoma as a rare epithelial tumor of the jaw, a variety of odontoma, arising from the enameloblasts and having no constant microscopic picture. The cell-type is the basal cell, but there may be all degrees of differentiation of the enamel organ. The undifferentiated forms consist entirely of basal cells.

Ewing[2] states "tumors of this group arise from paradental epithelial debris. Solid or cystic growths are located within the alveolar borders, the former tumors, as a rule, being more cellular and malignant. That all of these tumors are essentially of one nature is indicated by the numerous intermediate forms described in the literature and by the occasional transformations of unilocular types into multilocular, cystic or solid tumors in recurring cases (Guibout, d'Amients, Mallassez).

"Glandular adamantinoma (adenocarcinoma) covers a variety of structures in which columnar enameloblasts predominate. The lower jaw is the chief seat of cystic tumors (Pincus) while the upper yields most of the solid and more malignant growths. Tumors of the upper jaw are the more serious and the solid adamantinomas of all types recur locally and invade antrum, orbit and nasopharynx."

Robinson[3] in his survey of the literature, defines "ameloblastoma" as an epithelial tumor arising from the odontogenic apparatus or from cells with a potentiality for forming tissues of the enamel organ." This becomes the simplest and most sufficient definition of all when one notes the word "potentiality." The possibility of formation is present, but tissues of the enamel organ need not always be formed.

Some authors believe that this tumor may arise from the mucous membrane or from the mucous glands of the mouth.

All authors seem to be in accord in that the commonest sites of occurrence are the mandible, maxilla, tibia and hypophyseal body, probably in that order. The craniopharyngeal duct is derived from

the embryonic oral epithelium from which the dental lamina and the embryonic enamel organ also arise.

In 295 cases cited by Robinson, 83.7 per cent of the tumors occurred in the mandible while only 16.3 per cent occurred in the maxilla. In Ch'in's[4] series of 41 cases in the Chinese, 32 arose in the mandible, six in the maxilla and the site of three is not specified. Ch'in believes that the "glandular adamantinoma" is the rarest of all types and quotes Ghosh[5] in stating "the rarity of adamantinoma in the maxilla is due to better drainage of septic dental conditions in the upper than in the lower jaw." The tumor is invariably preceded in its origin from the jaw by some form of dental trauma.

Either the tumor arises as a solid growth and becomes cystic or it arises as either a solid or cystic type and so remains. There is evidence supporting the former controversial opinion. Ch'in states that the multiple cyst formation of both gross and microscopic dimensions, so characteristic of adamantinoma, is due to degeneration and disappearance of the central stellate cells probably as a result of nutritional disturbance since they are farther away from the vascular supply. Whatever the cause for transformation Robinson and Wallace[6] extirpated a solid growth and noted its recurrence five years later in a cystic form. The 1930 observations of Kronfeld were advanced in further writings of Robinson.[7] The tumor in Case 1, observed for five years, might have been solid becoming cystic later, while the tumor in Case 2 was removed in a solid form after existing for about the same length of time, as noted in the patient's history.

There is wide age incidence for this tumor but the greatest incidence is observed in the late third and early fourth decade of life. Ch'in observes that the decade from 20 to 30 has the highest incidence in the Chinese. Havens[8] observed that the fourth decade had the highest incidence in 58 patients admitted to Mayo Clinic.

Mosher,[9] Golden,[10] Phelps[11] and Androp[12] reported cases involving the antrum in individuals aged 61, 52, 42 and 43 respectively. It would appear that the age of strict sinus involvement is beyond the average of 37.6 years quoted by Robinson[3] or that of 38.3 years quoted by Bernier[13] for all locations.

Adamantinoma, like other antral tumors, may be suspected by a careful history which elicits earlier dental trauma and a unilateral nasal obstruction of long standing with mucopurulent or serosanguineous discharge. Also noted are symptoms of fetor, occasion-

ally frontal headache, cranial nerve disturbances involving the first, second, third, fourth, and fifth nerves, and external deformity. Case 1 presented a number of these symptoms. His external deformity consisted of obliteration of the nasolabial angle, was not pronounced and was attributed by the patient to the earlier kick of a horse.

Chont[14] believes that adamantinoma is quite characteristic roentgenologically. He believes that the solid adamantinoma produces a monocystic appearance on the x-ray film, and that it is interrupted by small niches on the border of the bony defect. This produces a more or less lobulated appearance and a few fine bone trabeculae to differentiate it from odontogenic cysts with their smooth borders. The polycystic type reveals a honeycomb appearance in the early stage. Tooth elements may or may not be contained, but the round, cystic compartments are quite characteristic.

The roentgenologic diagnosis of any antral tumor depends upon the familiarity of the roentgenologist with the behavior of the tumor in that location. Certainly all adamantinomas do not necessarily come encapsulated in a bony shell, nor produce large, bulging external deformities.

Roentgenograms in Case 2 show nothing of significance other than bone destruction, while those in Case 1 present certain characteristics outlined by Chont. A monocystic appearance is seen in those in Case 1, taken on February 25, 1941, with small niches in a bony trabecula through the midportion of the sinus while the successive films reveal a honeycomb appearance with round, cystic compartments. These findings are not entirely explained on the basis of displacement of air within the sinus, the ethmoid cells and other landmarks of sinus roentgenology.

Punch, aspiration or biting biopsies are not adequate for correct diagnosis of antral neoplasm. Ch'in believes that in biopsies of these three types the microscopic section may happen to show only structures resembling cystic adenoid epithelioma, cylindroma or mixed tumors of the salivary gland but the characteristic adamantinomatous structure will be found if sufficient material is obtained for study.

Certainly a Caldwell-Luc operation should have been done in Case 1 at a much earlier date in the face of his nasal findings, the questionable diagnosis of neoplasm and the desire to furnish the pathologist sufficient material for tissue study. Although we have

no stellate cells, columnar enameloblasts or adamantinomatous structure in this case, the diagnosis was only established when the antrum was curetted. Biting biopsy had produced three diagnoses, in which mucosa had figured twice; in the other a small projection of tumor through the sinus ostia had been taken and interpreted as well as possible in view of the amount of tissue received for study. The treatment of adamantinoma depends upon the age of the patient and the stage of the tumor at the time of recognition. Robinson reported 119 recurrences in his survey due to inadequate early removal. Hemisection, radical antrotomy and the type of treatment followed in the first case apparently afford the greatest opportunities for patient survival. Hemisection is poorly tolerated in the aged, but was well tolerated in the second case.

As Robinson and Wallace point out, the stage at the time of recognition is important. If the tumor is recognized and removed in the solid state, then enucleation and cauterization may suffice but if the cystic transition has begun and the interlamellar osseous spaces have been invaded by the tumor, then hemisection is the only treatment affording a good prognosis. Hemisection, of necessity, is an anatomically meticulous procedure and avulsion of structures should never be attempted. Surgical diathermy is often used in the hemisection.

Kimm and Baranoff[15] recommend hemisection and Havens believes that the tumor is a malignant one and that successful treatment depends upon early and radical removal.

The concensus is that irradiation affords little or no benefit in halting the progress of the tumor. Kimm[16] believes that the fully differentiated type of adamantinoma is highly radioresistant to x-ray or radium or a combination of both, while the basal cell type of undifferentiated tumor is comparatively radiosensitive. Kimm employed interstitial radon therapy (7200 r or 4263 m.c.h.) and found viable tumor cells remaining.

Berkove[17] reported recurrence following irradiation. In Eckhoff's[18] case the tumor responded to 2100 r in a very early stage while in only three of Chont's eight cases did the tumor respond to dosages of 1600 to 2400 r. Recurrence had not been reported in a case described by Davis,[19] although the elapsed time between discovery and the report had not been sufficient to allow for possible recurrence.

Surgery may be followed by irradiation in early stages although the most important feature of treatment is early, adequate and

radical surgery. Prognosis is directly reflected by the stage of recognition and removal of the tumor. The tumor is not benign in any sense.

Ewing believes that the prognosis in solid forms of adamantinoma is unfavorable regardless of the benign appearance of the cells. All authors indicate the tendency for these tumors to metastasize. Phelps' case exhibited definite evidence of metastases to the liver, lungs and ribs and clinically to the left retina. Death occurred approximately 13 months after discovery of the tumor. Kau and Wong[20] reported a case similar to the first reported here. In Androp's case the tumor extended intracranially from the left maxillary sinus to the frontal lobe of the brain with thrombosis of the lateral venous sinus.

McGregor[21] cites 28 cases of malignant adamantinoma in reviewing the literature. Of these 10 had metastasized, 13 were purely invasive and five were deemed malignant on microscopic examination, although the absence of constant microscopic pictures make the prognostication of malignancy rather difficult. McGregor regards as suspicious evidence of malignancy and constituting the atypical microscopic features of her eleven cases: Stroma with cells as dark as in some cases as fibrosarcoma; predominance of cuboidal over stellate and cylindrical types of cells, or predominance of epithelium over stroma with intertwining of epithelial processes. Only two of these eleven cases involved the antrum.

All diagnosed cases of adamantinoma must, for a favorable prognosis, be recognized early, be radically and thoroughly treated and watched frequently for any recurrence. Sufficient space should be created, by less radical surgical procedures in the aged, to allow for expansion of the recurrence that is ever a possibility.

CONCLUSIONS

1. The common name for the tumor is adamantinoma.

2. The tumor may be diagnosed in individuals beyond the fourth decade of life by a combination of nasal, roentgenologic and pathologic studies.

3. Pain may be a prominent symptom in any stage of tumor growth.

4. There are no characteristic microscopic features for all tumors grouped under the classification of adamantinoma.

5. Punch, aspiration and biting biopsies should be replaced by a Caldwell-Luc exposure when a tumor of the antrum is suspected.

6. The tumor is malignant, invasive and comparatively slow growing.

7. The treatment preferred by all authors is early and radical surgery.

8. The prognosis depends upon early diagnosis by the otolaryngologist.

PRESBYTERIAN HOSPITAL.

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LXXXIV

ADVANCED CARCINOMATA OF THE FACE

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Carcinomata of the face of a low grade of malignancy become advanced either through neglect or because of inadequate or improper treatment. Those of a high grade of malignancy may become advanced because of the very nature of the tumor, regardless of the treatment administered.

In their book on cancer of the face and mouth, Blair, Moore and Byars[1] state, "The death of a patient under treatment is not only a lamentable failure as regards that individual, but possibly worse—makes a bad mark against surgery that may deprive others of proper treatment at a time when it would be worth while". This statement is entirely true, and the same point of view may apply to unsuccessful surgical treatment following improperly chosen cases. However, it is equally undesirable to take a fatalistic attitude and advise only palliative treatment for those cases of advanced carcinoma which may have a reasonable chance of being cured. Consequently, the responsibility of the surgeon in selecting the method of treatment is at least as great as the actual carrying out of the treatment.

Probably the most important consideration in determining the proper method of treatment is an understanding of the degree of malignancy. While a large basal-cell epithelioma of ten or more years' duration, with or without previous attention, may be completely eradicated, an undifferentiated squamous-cell epithelioma of high grade and of only a few months' duration may present a most discouraging outlook.

As a rule, if all methods of treatment are available, there is a certain method or combination of methods that is most suitable for each case. Surgical removal with the cold knife or with electrocoagulation and irradiation with either roentgen rays, radium or radon are the most efficacious methods of treatment at the present time.

A basal-cell epithelioma which has not previously been treated and which has not involved the periosteum or the perichondrium

may be excised successfully with the cold knife. This type of tumor will respond well to irradiation also, but a certain number of them are mixed with a well-differentiated squamous-cell epithelioma which is radio-resistant. Since with irradiation therapy the entire tumor is not available for microscopic examination, the exact nature of the tumor may be unrecognized until the best chance of cure by simple measures is lost.

If the tumor has been treated unsuccessfully, particularly with irradiation, or if the periosteum or the perichondrium has become involved, thorough destruction by electrocoagulation is the method of choice. The wound is left open for persistent observation until recurrence is thought to be unlikely. Suitable procedures of a reconstructive nature can then be carried out.

The same circumstances and indications which are mentioned above for the treatment of basal-cell epitheliomata are applicable to the well-differentiated squamous-cell epitheliomata of low grade, except that since these tumors are radio-resistant, irradiation should have very little place in their treatment.

The percentage of cure of undifferentiated carcinomata of high grade is not high, regardless of the method of treatment, because of the very nature of the tumor. However, since these tumors are radio-sensitive, the use of irradiation is indicated. This may be the only method of treatment used in these cases or it may be combined with surgical procedures. This should depend on certain circumstances peculiar to each particular case.

An attempt is made to illustrate some of the above principles in the following case reports:

REPORT OF CASES

CASE 1.—A 35-year-old white woman presented herself at the Henry Ford Hospital with a basal-cell epithelioma which involved the left cheek and maxillary antrum. This had been present for ten years, during which time several attempts at removal had been carried out. An undetermined dosage of roentgen rays had been given also (Fig. 1).

On May 1, 1942, extensive electrocoagulation of the tumor was carried out. On three subsequent occasions it was necessary to electrocoagulate recurrences of the tumor, the last being on October 9, 1942 (Fig. 2).

Fig. 1.—Basal cell epithelioma, ten years' duration.

Fig. 2.—Thirteen months after electrocoagulation.

Fig. 3.—Appearance at present.

On November 1, 1943, 13 months after the last recurrence was electrocoagulated, repair of the postoperative defect was begun by the use of a lined flap from the forehead. On November 29, 1943, the flap was transferred to the cheek.

At present, 29 months after the last recurrence, there has been no further evidence of recurrence. The patient is wearing false dentures and is employed. Closure at the left corner of the mouth is not quite complete, but causes no inconvenience (Fig. 3).

In connection with this case it is interesting to note that Hertz and New[2] found that 44 patients under 30 years of age had been

Fig. 4.—Basal cell epithelioma of seven years' duration. No previous treatment.

treated for malignant disease of the face over a 24-year period at the Mayo Clinic. Of the 21 patients who were traced, 71.4 per cent had lived ten or more years after treatment.

CASE 2.—A 56-year-old white woman was examined on July 15, 1943. There was present a large fungating tumor involving the entire nose and obstructing the vision of the left eye. This had begun as a small pimple on the left side of the nose seven years previously and there had been no treatment for it. A small specimen for biopsy was taken which was found to be basal-cell epithelioma (Fig. 4). Roentgenograms of the chest revealed an old healed tuberculosis involving both hilar areas, both apices and both upper lung fields.

On July 23, 1943, the entire nose was removed with surgical diathermy and the base thoroughly electrocoagulated. Local infiltration of 2% novocaine anesthesia was used. Fifteen months later there was no evidence of recurrence. At that time there was some question of activity of the pulmonary tuberculosis, so plastic repair was postponed. The patient has returned to her native state and recent attempts to contact her have been unsuccessful.

CASE 3.—A white man, aged 51, presented himself at the Henry Ford Hospital on June 23, 1945. He complained of a "sore" that

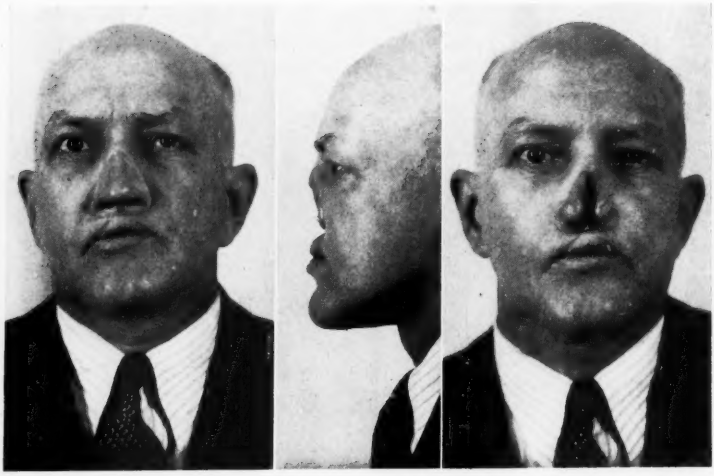

Fig. 5.—Appearance at present with prosthesis.

Fig. 6.—Appearance at present.

Fig. 7.—Appearance at present.

had been present in his nose for 18 months. For some time he had been under the care of a physician who had treated him with salves, sprays and "light treatment." On examination of the nose a large tumor could be seen involving both sides of the nasal septum and the inner surface of the alae. The external appearance of the nose was perfectly normal. There was a firm palpable gland, about 2 cm. in diameter, in each submaxillary triangle. No other significant abnormalities were noted. Roentgenograms of the chest showed no evidence of metastasis. The blood Wassermann test was negative. A biopsy showed squamous-cell carcinoma, grade II.

On July 2, 1945, with deep cervical block anesthesia, a bilateral submaxillary and submental cervical gland dissection was carried out. Following this, with infiltration anesthesia of 2% novocaine, the tumor, involving the lower half of the nose, was thoroughly electrocoagulated.

Microscopic examination of the cervical lymph glands revealed metastatic carcinoma in a gland from each submaxillary triangle.

On July 15, 1945, two weeks later, it was necessary to electrocoagulate an extension of the tumor on the upper lip which had been incompletely removed at the first operation (Figs. 6 and 7).

Since there was metastic involvement of the superficial lymph nodes on both sides and since none of the deeper nodes were palpable, further operative procedures were deferred. However, in April 1946 the upper deep cervical nodes on the left became palpable, so on May 3 block dissection of the cervical glands on the left was carried out. This procedure will be carried out on the right side in the near future.

Considering the moderate activity of the tumor, and the fact that cervical metastasis had taken place, the probability of recurrence is thoroughly appreciated. However, it is felt that this case illustrates clearly the tragedy of neglect and the value of surgical treatment, even in a moderately active and advanced carcinoma.

A prosthesis has been prepared from Dicor, a soft plastic. This gives him quite a bit of comfort from a psychological standpoint, especially since he is employed (Fig. 5).

HENRY FORD HOSPITAL.

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LXXXV

EOSINOPHILIC GRANULOMA

REPORT OF A CASE INVOLVING THE FRONTAL BONE

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The purpose of this paper is to review briefly the recently accumulating literature on eosinophilic granuloma, and to report an unusually interesting case involving the frontal bone.

Jaffe and Lichtenstein[1] define eosinophilic granuloma as "a condition affecting one, several or many bones, but apparently limited to the skeleton, and representing the mildest clinical expression of the peculiar inflammatory histiocytosis also underlying Letterer-Siwe disease and Schuller-Christian disease." Eosinophilic granuloma was at first considered a solitary lesion[2, 3, 10] but it is now known that multiple lesions may be present although the presenting complaint may result from the lesion of one bone while other lesions may be clinically inactive.[1, 4, 7]

Green and Farber,[5] Mallory,[6] Jaffe and Lichtenstein[1] and others have shown that the underlying lesion of this disease is related to the lesions of Schuller-Christian disease and of Letterer-Siwe disease, the latter representing the gravest and eosinophilic granuloma the mildest expression of the same basic pathological process which appears to have a predilection for the hemopoietic system. When this "peculiar inflammatory histiocytosis" manifests itself in infancy in its severe and often fatal form—characterized clinically by fever, purpuric skin rash, rapidly progressive hypochromic anemia, enlargement of the spleen, liver and lymph glands, and by destructive bone lesions—it is classified as Letterer-Siwe's disease ("aleukemic reticulosis," "non-lipoidal histiocytosis").

In its more chronic and less severe form, occurring in childhood and early adult life, after the lesions of the soft tissues and the

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bones have undergone lipogranulomatous changes, and especially—though not characteristically—when the Christian triad of symptoms (calvarial defects, exophthalmos, and diabetes insipidus) has developed, then the disease is labeled Schuller-Christian disease ("lipogranulomatosis").

Eosinophilic granuloma is the mildest of this group of three rare diseases and its lesions appear to be limited to the skeletal system. It is a disease of early life, more frequent in males, which may affect any bone or group of bones, being most common in the bones of the cranial vault, the ribs, vertebrae, and long bones. In half of the reported cases the skull has been involved, either alone or in combination with other bones.[12] It may first involve one bone and later other bones, producing localizing symptoms which may vary from a mild local tenderness and pain or disability to multiple neurological signs and symptoms;[8, 9] or the disease may escape clinical detection until discovered incidentally. In our case the clinical picture was that of a chronic sinusitis with mucocele of the ethmoid. The condition is rarely associated with any systemic symptoms. Infrequently the disease may be ushered in by a slight fever and occasionally there may be a mild leucocytosis or an eosinophilia of four to ten per cent.

The etiologic organism has not been identified nor isolated. Studies of blood phosphorus, calcium, phosphatase, blood lipids, cholesterol, proteins, serologic tests for syphilis, and urine tests for Bence-Jones proteins have failed to throw any light on the etiologic agent.

Roentgenographically, the lesions appear as radiolucent areas varying in size. In the skull they tend to be rounded, sharply defined, and having a punched-out appearance. Solitary lesions may resemble bone cysts, mucoceles, osteomyelitis or malignant disease. Multiple lesions may suggest cancer, multiple myeloma or Schuller-Christian disease. Thus, there is nothing distinctive about the roentgenographic appearance. The diagnosis must be based on histological examination following surgical excision or curettage.

For a detailed description of the gross and microscopic pathology the reader is referred to the excellent paper of Jaffe and Lichtenstein.[1] In brief, the basic lesion appears grossly as a "more or less hemorrhagic and cystic area from which only a small amount of granulation tissue can be curetted".[1] Microscopically it is characterized by numerous histiocytes strikingly infiltrated with eosinophiles and containing multinucleated giant cells, the whole having

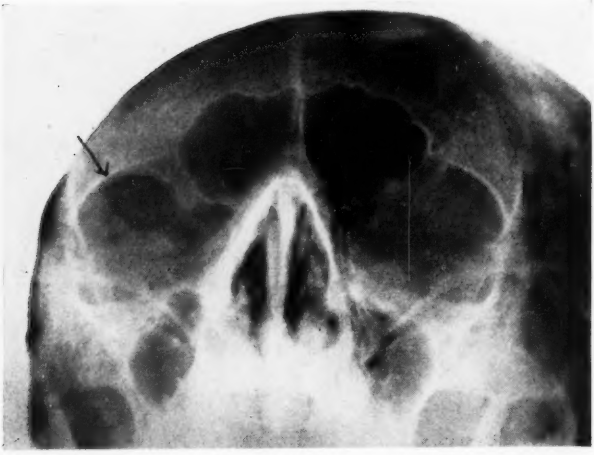

Fig. 1.—Roentgenogram showing preoperative defect in roof of right ethmoid, suggesting diagnosis of mucocele.

Fig. 2.—Postoperative roentgenogram showing extent of bone removed.

a granulomatous appearance in which the histiocytes represent the basic component and the eosinophiles the most striking.

The treatment is surgical excision or curettage of the solitary lesion and x-ray irradiation for multiple lesions. Green and Farber[5] recommend 1500 r units, through two fields, in divided doses over a period of six days. Spontaneous healing may occur. The prognosis is excellent.

Our patient, S. L., a 21-year-old female, was admitted on the Nose and Throat Service of the Massachusetts Eye and Ear Infirmary on January 4, 1946, complaining of right frontal headache, diplopia and swelling about the right eye.

Past History: The patient had always been in good health and except for an appendectomy in 1938 had had no need for medical attention. There were no complaints referable to the nose and throat prior to the present illness.

Present Illness: About two and a half months prior to admission, shortly after a mild head cold, the patient first noted right frontal headache radiating to the temporal region. The headache was fairly constant. Stooping produced a sensation of dizziness and straightening up caused sharp pain to dart to the frontal and temporal areas. There was no associated nasal obstruction or discharge, chills, fever, or malaise.

Four weeks prior to admission the right upper eyelid and brow became puffy. The right eye appeared to be pushed downward and occasional diplopia was noted.

One week prior to admission the diplopia became more annoying and the swelling of the upper lid and brow region became more marked, with some reddish discoloration of the upper lid. This had been gradually subsiding just prior to admission.

Physical Examination: The patient was a well-developed and well-nourished adult female in no apparent distress. Her temperature was 98.6, pulse 90, respiration 20. The right eyelid was mildly edematous and the eyeball showed slight proptosis and downward displacement with motion reduced upwards. The pupillary reactions were normal, the fundi were normal, and the eyeball was slightly tender on pressure. The nasal mucosa was normal in color and the airways were clear. There was scant mucoid discharge in the right naris; no postnasal drip. The mouth, pharynx and larynx were normal. The sinuses were not tender and were clear on tran-

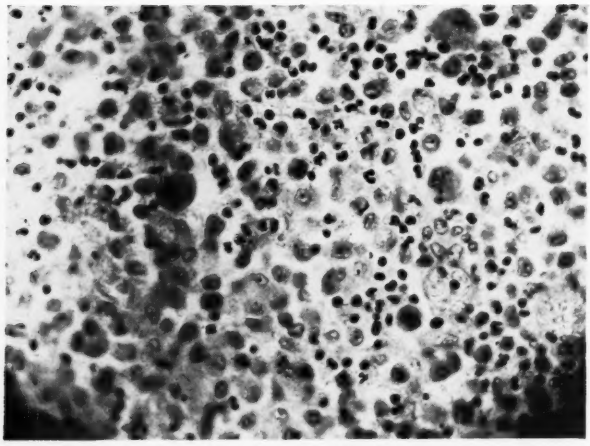

Fig. 3.—Photomicrograph showing a cellular "tumor" characterized by relative absence of stroma, infiltration with histiocytes and polymorphonuclear leukocytes (eosinophiles) and an occasional giant cell. (x235)

sillumination. Her blood pressure was 120/80. The remainder of the physical examination was essentially negative.

Laboratory Findings: The white blood count was 6,200 with 71% neutrophiles, 24% lymphocytes, 4% monocytes, and 1% basophiles. The red blood count was 5.3M; normal morphology, hemoglobin 14.3 gm. Urine was negative; the Hinton test was negative. Nose culture: coagulase positive hemolytic streptococci. Throat culture: coagulase positive staphylococcus aureus and alpha hemolytic streptococci.

X-ray Examinations: X-ray films of the sinuses show, "There is an opening in the roof of the right orbit, probably due to a mucocele of the ethmoid. It may have become infected." X-ray films of the skull, the spine and the pelvis (taken postoperatively, on February 9, 1946) show, "There is no demonstrable evidence of metastatic malignancy. There is slight anterior narrowing of the body of the eighth dorsal vertebra which has the appearance of an old postural change. It is not due to a pathological fracture."

Clinical Diagnosis: Mucocele, right ethmoid, eroding through the roof of the orbit.

Operation: The patient was given 20,000 units of penicillin every 3 hours and on January 7 a right external frontal and ethmoid operation was performed under intratracheal, ether anesthesia.

The usual Lynch incision was made through the right eyebrow curving down onto the nose. The periosteum was elevated and reflected. The frontal sinus was entered through the floor and found filled with polypoid membrane and secretion. The bony floor of the frontal sinus was removed entirely, including the posterior and external boundaries and all membrane was removed. Enough of the anterior-inferior bony wall of the sinus was removed to enable one to see that there were no lateral extensions and that the inter-frontal partition was intact. As the orbital periosteum was further reflected over the entire roof of the orbit, there was noted in the outer part of the bony roof of the orbit what appeared to be a meningocele, one half inch in diameter. This was separated from the external confines of the frontal sinus by a strip of healthy bone one centimeter in width.

The edges of the suspected meningocele were freed from surrounding bone with difficulty and then a semi-soft mass could be wiped and teased off the dura, leaving fairly healthy looking dura.

All the anterior and posterior ethmoid cells were diseased and were completely exenterated and the wound was closed without drains.

Biopsy Report: "Eosinophilic granuloma of the orbital plate of the frontal bone. An irregular piece of tissue measuring 15 x 10 x 5 mm. (in Zenkers)."

Postoperative Course: The patient had an uneventful convalescence. The wound healed by first intention. The note made on her discharge January 15, 1946 reads. "External wound well healed without deformity. No tenderness, headache, or diplopia. Slight crusting right naris. Patient feels very well." The follow-up note made on March 8, 1946 reads: "Patient entirely asymptomatic, appears and feels well."

The patient was given a total of 500 r units of x-ray over the right frontal and ethmoid region in two doses (February 15, 1946 and February 28, 1946), 200 k.v. being given through a .8 cm. portal. The right eye was protected with lead during treatment. The patient will be observed for possible occurrence of other bone lesions.

SUMMARY

1. The literature on eosinophilic granuloma is briefly reviewed.

2. A case is reported, showing a solitary lesion located in the right frontal bone, apparently eroding the roof of the orbit and lying against the dura and presenting the clinical picture of a mucocele of the ethmoid with secondary infection. Surgical excision followed by x-ray irradiation gave an excellent result.

243 CHARLES STREET.

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LXXXVI

SALIVARY GLAND TUMOR OF THE LIP

LEON L. TITCHE, M.D.

TUCSON, ARIZ.

Several reports have appeared in the literature noting the occurrence of normal salivary gland tissue outside of its usual locations. None of these mentioned its appearance in the lip and for that reason we consider that our case may be of interest.

W. C. G., a white male aged 22 years, reported to the Clinic on April 3, 1946, for treatment of a small mass on the inner surface of the right side of the lower lip, which he had noticed first about three weeks previously. The mass was not painful, but had increased slightly in size and bothered him in that he was biting it. Examination revealed on the inner surface of the lower lip to the right of the midline, a slightly elevated, firm mass measuring 1 by 2 cm. The mass was not tender, was covered by normal-appearing mucous membrane, and was freely movable. There was no local or cervical lymphadenopathy.

On April 9, 1946, the mass was excised under novocaine infiltration anesthesia. Incision of the mucous membrane resulted in extrusion of a pinkish-gray tissue. A distinct line of cleavage was found and the mass was completely removed without difficulty. No unusual bleeding was encountered and the incision was closed with interrupted silk sutures. Healing was rapid and was complete in seven days.

The tissue removed was submitted for pathological examination and the following report was received: "Microsections reveal salivary gland tissue which is normal in all respects. There is no evidence of marked dilatation of ducts but these sections do not contain any of the larger ducts of these glands. Diagnosis: Normal salivary gland tissue" (Fig. 1). Further study of the sections revealed the presence of both mucous and serous secreting cells, similar in structure to those found in submaxillary, sublingual and labial glands.

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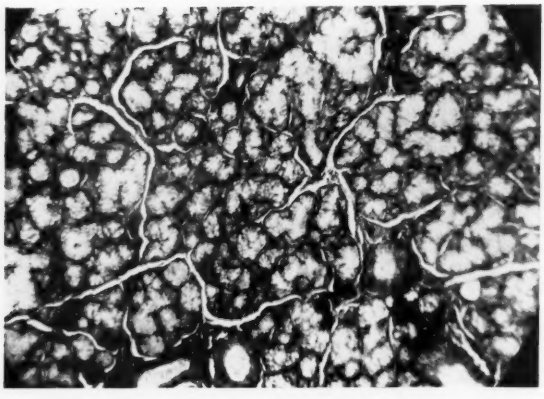

Fig. 1.—Photomicrograph of tumor. (X 55)

DISCUSSION

Normal salivary gland tissue has been found in the tonsillar fossae after tonsillectomy by Neumann,[6] Tillotson,[11] Seydell,[8] Prohovnik,[7] Armstrong,[1] and Hitschler and Cope.[4] Stratton[9] found salivary gland tissue on the hard palate and mentioned that other authors had found it on the gums. Eggers[2] reported one instance of this type of tissue in the pharynx. Mixed tumors of the parotid gland have been found on the hard and soft palates, pharynx, gums, and lips.

While there have been instances of normal salivary gland tissue appearing in what seemed to be outside of its normal locations, these may have been normal. In Gray's Anatomy[3] we find the following: "The labial glands are situated between the mucous membrane and the orbicularis oris, around the orifice of the mouth. They are circular in form and about the size of small peas; their ducts open by minute orifices upon the mucous membrane. In structure they resemble the salivary glands." Jordan[5] classifies the labial glands as belonging to the mixed type of salivary glands. Thoma[10] mentions mucous cysts of the lower lip due to occlusion of the outlet of a labial mucous gland and the occurrence of mixed tumor of the lip, but he does not give any instances of benign hypertrophy of the labial glands.

The explanation of the occurrence of the salivary gland tumor of the lip in our case is either that it is a hypertrophy of the tissue of a labial gland or that it is the result of embryonic displacement of an anlage of a salivary gland.

SUMMARY

A case of a salivary gland tumor of the lower lip is described. If all instances of this condition were reported, it is possible that it would be found not to be as infrequent as it appears.

The author wishes to express his appreciation to Dr. R. B. Streets of the University of Arizona for the preparation of the photomicrograph.

VETERANS ADMINISTRATION.

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Society Proceedings

SIXTY-SEVENTH ANNUAL MEETING

OF THE

AMERICAN LARYNGOLOGICAL ASSOCIATION

Chicago, Ill., May 29-30, 1946

THE PRESIDENT, DR. HAROLD I. LILLIE, PRESIDING

(Abstracts of Proceedings)

Osteomyelitis of the Maxilla Secondary to Suppurative Maxillary Sinusitis

HAROLD I. LILLIE, M.D.

ROCHESTER, MINN.

(This paper appeared in full in the September issue, page 495)

Rhinosporidiosis

FRANK R. SPENCER, M.D.

BOULDER, COLO.

(This paper appeared in full in the September issue, page 580)

DISCUSSION

DR. JOHN J. SHEA commented on the difficulty of culturing the spores, which has resulted in much confusion among mycologists. Dr. Shea reports having seen two cases of this disease, in one of which the tumor mass was attached to the septum. A specimen sent to the Army Museum's laboratory was reported as a "plasmocytoma." Dr. Shea showed a slide which depicted a foreign body granuloma about the spore. The central body of the spore is a chromatin body

which multiplies many times and then ruptures as the body is forced to the surface. Fragments of the rupture chromatin are thus deposited in the tissue, causing an increase in the size of the lesion and the production of new granulomata.

DR. H. V. PENTA called attention to the similarity between the histopathologic picture in the slide shown by Dr. Spencer with that of coccidioides immitis. The latter, like the former, grows by forming endospores which rupture when the tension reaches a certain point. Dr. Penta stated that he has seen lesions of this type in the skin.

Cleft Palate and Lip

HUGH G. BEATTY, M.D.

COLUMBUS, OHIO

(This paper appeared in full in the September issue, page 572)

DISCUSSION

DR. WARREN B. DAVIS mentioned the variety of procedures employed in these cases with the same end in view. He called attention to the present trend toward operating earlier in life than formerly was the case. As a rule these operations are now being done at the age of 15 to 20 months. He agreed with Dr. Beatty on the importance of preoperative care and stressed particularly the elimination of ethmoid disease which, in his experience, has contributed to the incidence of postoperative infection. He differs with Dr. Beatty on the point of the one-stage operation, preferring to do it in two stages. It is his contention that the child can stand two short operations better than one long one. Besides, it affords some time for the establishment of collateral circulation.

Based on an experience with 4,600 cases since 1913, Dr. Davis feels that he has obtained better results with osteoplastic flaps than with mucoperiosteal flaps. There is less scar contraction in the former. Also he is convinced that in the two-stage operation the mortality is lowered, greater length is obtained in the palate and the resulting voice is better.

DR. THOMAS E. CARMODY agreed on the importance of x-ray studies of the thymus but did not feel that they are needed after the age of two years. He has not had as much success with osteoplastic flaps as Dr. Davis and follows pretty closely the technic described by Dr. Beatty.

Dr. Carmody finds that the feeding problem is materially improved by the use of intravenous glucose solutions given for the first five or six days. He agrees with Dr. Beatty that narcotics should not be used in these cases; neither does he approve of the use of atropine.

Like Dr. Beatty, Dr. Carmody elevates the mucoperiosteum and also splits the soft palate as described by Gilbert. However, instead of using catgut sutures he employs horsehair or some other nonabsorbable material.

Dr. Carmody is conscious of the role of the sinuses in secondary infection and also calls attention to the possibility of infection passing up the eustachian tube to the middle ear, because of the prolonged position of the child on its back. Cooperation on the part of the pediatrician and careful nursing can do much to mitigate such complications.

DR. FRANCIS L. LEDERER emphasized the importance of the effect of the operation on the speech mechanism. Careful attention to speech training has in some institutions resulted in 70 per cent of the credit ascribed for good results in this direction.

DR. F. R. SPENCER stated that the service of speech therapists in the medical school at Denver has proven of inestimable value in the follow-up of these cases.

DR. BEATTY, in closing, agreed that speech training is highly important. It is one reason why early operation before bad speech habits are developed is so essential. However, it may all come to naught if the operation itself leaves the patient with a short, scarred palate or one that is imperfectly attached.

The Danger of Unrecognized Anoxia in Otolaryngology

THOMAS C. GALLOWAY, M.D.

EVANSTON, ILL.

(This paper appeared in full in the September issue, page 508)

DISCUSSION

DR. HENRY M. GOODYEAR stated that there is a definite relationship between juvenile delinquency and whooping cough occurring in infants under two years of age. This was corroborated by observations made in a hospital for delinquent children. This would seem to be a good argument in favor of early inoculation against this disease. Dr. Goodyear believes greater care should be exercised in the administration of anesthetics to young children for the removal of tonsils and adenoids. If nitrous oxide is used for induction a sufficient amount of oxygen should be given to counteract a possible mild anoxia. Also, the anesthetic should be withdrawn early even if there are signs of impending emesis.

DR. FREDERICK T. HILL believes the important factor in surgical shock is tissue anoxia. He referred to some experimental work by Dr. Porthus at the New England Medical Center, in which it was shown that venous blood returning to the heart contains a certain amount of oxygen, and by using Cytochrome C it was possible to increase the tissue absorption of oxygen. Experiments on rats showed that even in severe degrees of anoxia the survival rate was markedly increased by the use of this medicament. In human beings it was observed that the visual disturbances of anoxia, the electrocardiographic and electro-encephalographic changes likewise could be prevented by preliminary intravenous administration of Cytochrome C. This element is derived from Vitamin B_1, is stable, nontoxic, and has been successfully employed in barbituric acid poisoning.

DR. W. LIKELY SIMPSON mentioned the importance of having a laryngologist serve as chairman of a committee of the staff to supervise the activities of the Department of Anesthesia.

DR. GORDON B. NEW asked one question regarding the group of poliomyelitis cases mentioned by Dr. Galloway in which tracheotomy was performed. In his experience with bulbar cases, fatalities usually resulted from involvement of the intercostals, and he wished to know in just what percentage of cases tracheotomy was

indicated, or how it was determined that certain other cases would ultimately recover without this procedure.

Dr. De Forest C. Jarvis called attention to the fact that natives living in the Andes Mountains at altitudes up to 16,000 feet were in the habit of eating the seeds of kelp obtained from the Pacific Ocean. This leads him to believe that the ingestion of oxidizing agents such as kelp, iron, manganese and copper, are effective in relieving anginal pains due to cardiac anoxia.

Dr. Galloway, in closing, agreed with Dr. Goodyear that delinquency in children might be due to periodic anoxia following whooping cough, as it is with mumps and atelectasis. He has also been concerned about the dangers of general anesthesia in children and was interested to hear Dr. Hill's statement concerning the use of Cytochrome C. In answer to Dr. New's question, he stated that the respiratory difficulty in bulbar poliomyelitis is described as of three types, paralysis of the intercostals and diaphragm, lack of rhythm and laryngeal paralysis interfering with swallowing. In the first instance there is no difficulty in swallowing fluids. Such patients do well in a respirator. As for arrhythmia, Dr. Galloway doubts its existence and believes the symptoms are due to fluid. In the laryngeal paralysis cases, fluid cannot be swallowed and it accumulates to the point where the patient may drown in his own secretions, especially if he is in a respirator, unless frequent aspiration is employed. Tracheotomy in such cases can prevent asphyxia by providing a short cut for facilitating the aspiration of fluids from the lower air passages. As a rule the laryngeal paralysis is of short duration and the swallowing function is restored in five to eight days. This is the crucial period when tracheotomy may prove to be a life-saving measure.

Some Causes of Hoarseness in Children

Francis W. White, M.D.

New York, N. Y.

(This paper appeared in full in the September issue, page 537)

DISCUSSION

Dr. Louis H. Clerf emphasized the importance of direct inspection of the larynx in these children. With patience this may be accomplished with the mirror, although in some cases direct laryn-

goscopy is necessary. In his experience most cases are due to screaming and yelling at outdoor sports. Treatment requires considerable tact and cooperation on the part of the parents and teachers.

DR. WHITE, in closing, spoke of the lack of cooperation by the patient and the family, especially if the condition is pronounced as not being dangerous. The services of a speech teacher may be of some assistance.

Aphonia

CARL H. MCCASKEY, M.D.

INDIANAPOLIS, IND.

(This paper appeared in full in the September issue, page 524)

DISCUSSION

DR. RALPH A. FENTON called attention to the physical changes which may appear in these cases and which require treatment. Too much emphasis on the psychological angle in young individuals may not be so desirable. Even in cases where the problem is principally a psychoneurotic one, the laryngologist should be able to solve the difficulty in most cases without the assistance of a psychoanalyst.

DR. ERNEST M. SEYDELL commented on the mechanism of the transference phenomenon and described his procedure of provoking a cough and putting the patient through humming exercises, followed by external finger pressure on the larynx and other suggestive procedures which, at his hands, have yielded excellent results.

DR. FRED Z. HAVENS, as well as Dr. Seydell, mentioned the high-pitched character of the voice in some of these cases which are not strictly aphonia but rather a form of dysphonia. They are treated by the same procedures as outlined by the essayist.

DR. GORDON F. HARKNESS emphasized the objective picture of functional aphonia in which the normal appearing cords, on attempted phonation, move inwardly but relax at the moment approximation is imminent.

DR. ROBERT C. MARTIN described a type of pseudo-aphonia encountered in aviators at high altitudes where the reduced air pres-

sure interfered with the sound of the voice over the "intercom." With the advent of the B-29 and its pressure chambers his difficulty was overcome.

DR. MCCASKEY, in closing, again emphasized the importance of getting to the bottom of the psychological complex which brings this condition about. Local therapy alone may result in only temporary improvement and relapses are common unless the patient and the family are convinced that the condition is not due to any local pathological condition.

Associated Paralyses of the Larynx

CLAUDE C. CODY, JR., M.D.

HOUSTON, TEXAS

(This paper appeared in full in the September issue, page 549)

DISCUSSION

DR. FRANCIS L. WEILLE brought out the fact that the bulbar cortical spinal tract differs from the pyramidal tract in that it decussates once, whereas the pyramidal tract decussates twice; that is, first, just above the cord at the beginning of the medulla and again lower down. Also, the question is asked as to whether the cranial portion of the 11th nerve supplies both cords through the 10th, it being his understanding that such was the case. Concerning the differentiation between spastic and flaccid paralysis in the larynx, Dr. Weille felt that the only way it could be done would be by inference from the status of the associated paralyses of other muscles.

DR. CODY, in closing, called attention to the fact that the controversy over the role of the 11th nerve in innervation of the larynx has been the topic of debate for many years, with no agreement in sight. It is difficult to trace all the fibers of the nucleus ambiguous, because by the time they reach the surface of the medulla their relative positions have changed. He is satisfied that in most cases that part of the nucleus ambiguous supplying the accessory nerve does not usually arise in the medulla, but in some such place as suggested by the Jackson, Schmidt and Tapia syndromes. It would be reasonable to assume in the presence of a torticollis associated with paralysis of the larynx, that the nerves arose from cells that were in close juxtaposition.

Intralaryngeal Operation for Selected Cases of Laryngeal Cancer

FRANCIS E. LEJEUNE, M.D.

NEW ORLEANS, LA.

(This paper appeared in full in the Setember issue, page 531)

DISCUSSION

DR. TAQUINO, who was associated with the late Dr. Lynch at a time when the latter was doing a number of intralaryngeal excisions, has followed this technic for a number of years and recalls having shown ten such cases of his own at the Graduate Medical Assembly in New Orleans two years ago; all of these patients were well and without recurrence for periods of from two to seven years. It has been his custom to do a wide excision followed by electrocoagulation of the base.

DR. FRED Z. HAVENS reported having successfully performed this operation in a few selected cases with excellent results. He feels that the procedure has a definite place in the laryngologist's armamentarium, but is not the sort of thing to be carelessly adopted. It requires not only skill of a high order but mature judgment in the selection of cases.

DR. SAMUEL SALINGER did not believe that the procedure described by Dr. LeJeune would be misapplied or substituted for more radical technics indiscriminately. In his own experience he has rarely seen the cases early enough to be amenable to it. He could recall only two instances in which it was employed: in one case because the patient refused an external operation and in the other because the lesion was so small that it was entirely removed by the biopsy. Both patients remained well. He believes that with increasing attention focused on the cancer problem through newspaper and magazine publicity, more cases might appear early enough for this procedure. He feels also that suspension laryngoscopy affords the best approach, since the field is thus widely exposed and both hands are free to work.

DR. C. C. CODY emphasized the importance of regarding all papillomas as potential cancers and recommends fulgurating the base after their extirpation. This also applies to the treatment of the raw area remaining after a simple biopsy. The resulting ulcer will heal better and with less danger to the patient.

DR. M. JACKSON (South Africa) recalled a case in which a papilloma removed from the anterior commissure proved to be malignant. Since laryngectomy was refused by the patient, Dr. Jackson removed the upper third of both cords and for three years the patient has remained free from recurrence. He asked Dr. LeJeune's opinion of this case.

DR. W. MCCALL stated that he has not been fortunate enough to see the cases as early as has been Dr. LeJeune's experience. The vast majority of his cases have required a laryngectomy. He would like Dr. LeJeune to state whether the question of limitation of motility of the cord plays any part in determining on this procedure or rejecting it.

DR. GABRIEL TUCKER, like the preceding speaker, has seen extremely few cases that would be amenable to this procedure. He has had the experience of removing a small lesion at biopsy and then at a subsequent laryngofissure found further evidence of carcinoma in the surrounding tissues. He feels that it is necessary to remove the internal perichondrium if the spread of the carcinoma is to be avoided, and this part of the technic can be better accomplished through a thyrotomy exposure than under suspension. He has found that a good voice may result even after wide excision of the cords, through the formation of a new adventitious cord. Also, since he has been using penicillin preoperatively and postoperatively in these cases, in addition to preliminary tracheotomy, the healing has been much smoother and recovery more rapid.

DR. JOHN H. FOSTER stated that in his part of the country (Texas and Louisiana) they do see a number of early cases which he believes may be attributed to publicity and the alertness of the family physician who refers them. Also, he approves of the suspension exposure. Furthermore, the technic, like that of fenestration, requires more than average skill.

DR. GORDON NEW, in reviewing a large series of cases of carcinoma of the larynx from the Mayo Clinic, found that 11 per cent were treated by endolaryngeal removal under suspension, thus proving that there is a definite indication for this technic. The end results were excellent as shown in a follow-up, which found 92 per cent of them living and well over a five-year period. The largest percentage in this group were low grade tumors, which is a factor that should be taken into consideration when a decision is to be made.

DR. A. H. ANDREWS, JR., suggested the use of the stroboscope for the early diagnosis of laryngeal carcinoma. He has found it possible to detect early infiltration of the cord by observing a rigidity either anterior or posterior to the growth, which interferes with the undulating ripple seen in the normal cord or in the presence of a small benign lesion.

DR. LEJEUNE, in closing, again emphasized the importance of proper selection of cases. The lesion must be small and surrounded by apparently healthy tissue on all sides. Replying to Dr. Cody, Dr. LeJeune stated he had never used the fulgurating current in benign papillomas. In the case of a flat papilloma that proved malignant he would certainly do a thyrotomy rather than the procedure he described. As for Dr. Jackson's case, he thought the technic that was carried out was correct and exactly as advocated by Jackson. Concerning Dr. McCall's question relating to limitation of motion in the cord, Dr. LeJeune believes such a finding indicates a wide-spread, deep-seated lesion which, in most cases, calls for a laryngectomy. Relative to Dr. Tucker's discussion, it is entirely a question as to whether the lesion is superficial or not. Endolaryngeal excision is only indicated in small superficial lesions of Grade I or Grade II type, and when properly indicated and carried out certainly mutilates the larynx much less than a thyrotomy and will result in better regeneration of the cord with better voice quality. He has never tried the stroboscope but believes there should be some merit in its use.

Intranasal Medication. An Investigation Into the Relative Merits of Certain Methods of Introducing Fluids Into the Nose

TERENCE CAWTHORNE, M.D.

LONDON, ENGLAND

(By invitation)

(This paper appeared in full in the September issue, page 519)

DISCUSSION

DR. ARTHUR W. PROETZ was not surprised that the solutions introduced in the head-upside-down position reached all parts of the nose, since this had been proven previously by x-ray studies with

lipiodol. However, he was surprised that the other methods employed were so relatively ineffectual. He inquired of the essayist as to toxic effects which might be expected from the introduction of a dram of 10 per cent cocaine solution left in situ for half a minute. This is a fairly large dose and the absorption must be quite rapid and considerable.

DR. CAWTHORNE, in reply to Dr. Proetz, stated that at first they did use weaker solutions but found they could not abolish olfactory function with less than a 10 per cent solution. Although there were no marked toxic effects in any of the subjects, a definite giddy exhilarating effect was observed which lasted for two or three hours. As far as he was able to determine there was no permanent damage.

Sensitivity from Insufflation of the Powdered Sulfonamides in Acute Infections of the Nose and Throat

HOWARD C. BALLENGER, M.D.

WINNETKA, ILL.

During a period of three years, from July 1, 1943, to July 1, 1946, approximately 6,000 insufflations of powdered sulfonamides, singly or in various combinations, were administered to about 1,500 individuals for various types of acute infections of the nose and throat. The average amount used for insufflation was .3 gm. Sensitivity as manifested by a dermatitis, hives or other allergic response was noted in seven cases. There were no known cases of sulfonamide resistence in this series. An average of about two and one-half treatments was given in each acute attack. Some of the patients were treated for two or more acute attacks during the three year period.

DISCUSSION

DR. RALPH A. FENTON has observed two instances of marked reaction to the use of powdered sulfonamides in the nose, manifesting itself in a dermatitis of the face. He asked whether Dr. Ballenger had seen anything of this nature in his series of cases.

DR. BALLENGER, in closing, stated that he accepted allergic patients if there was no history of sensitivity to sulfonamides. Such patients responded to the treatment the same as nonallergic patients.

Frontal Sinus Drainage

O. E. VAN ALYEA, M.D.

CHICAGO, ILL.

(This paper appeared in full in the June issue, page 267)

DISCUSSION

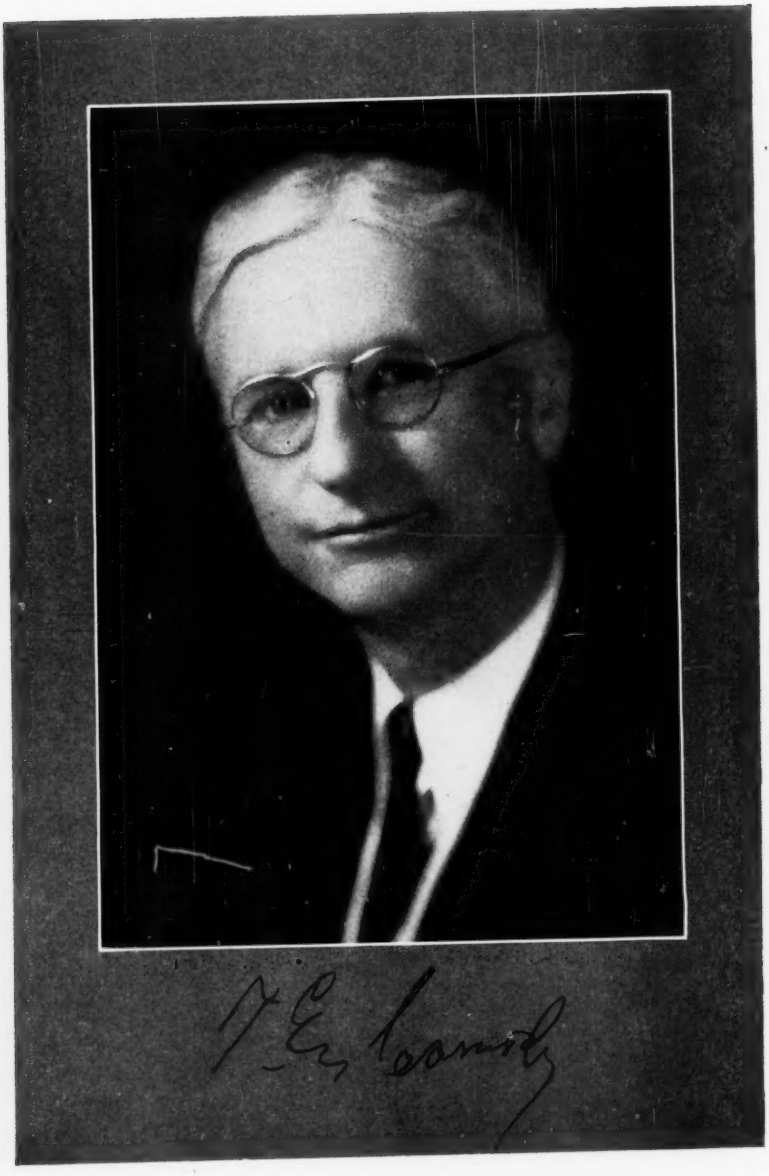
DR. BERNARD J. MCMAHON agreed that certain frontal sinuses can readily be cannulated and irrigated and that such therapy materially shortens the duration of the infection. In this connection, he called attention to the practice of mass suction at the anterior nares which is still practiced by some, and which can only do harm by drawing the edematous mucosa into the duct, causing increased obstruction. Also, the use of diathermy may be harmful because the increased circulation in the tissues only adds to the engorgement already present, causing more swelling of the mucosa. Experiments on animals proved that not only does the swelling increase but that capillary hemorrhages and hematoma may result. He feels that in acute cases every effort should be made to establish the patency of the duct by careful probing with finely wrapped applicators saturated with a shrinking solution. Also, he has found it helpful in acute cases to give the patient ephedrine and nembutal capsules.

Presentation of a Patient

SAMUEL SALINGER, M.D.

CHICAGO, ILL.

Dr. Samuel Salinger presented a young woman who had suffered from recurring, intractable hemorrhages from the nose over a period of years. The case had been reported to this Association two years ago and to date the etiology is still undetermined, except for the evidence pointing to self-inflicted trauma under compulsion of a deep psychoneurotic complex, which psychoanalysis has only partially resolved. The blood picture is one of a marked secondary anemia, which is being held fairly stationary by continuous medication. The nasal bones and the intranasal structures are markedly atrophied and most of the septum is gone.



THOMAS EDWARD CARMODY, M.D.

1875-1946

Thomas Edward Carmody was not merely an eminent otolaryngologist, he was likewise famous here and abroad for his admirable attainments in maxillo-facial, oral and plastic surgery. One had only to see him in the wards of the Children's Hospital, or with his colleagues at a medical meeting, to realize that his was a friendly character, devoid of ostentation or pretense.

Dr. Carmody was born and educated in Michigan. After graduating from the Dental School of the University of Michigan in 1897 he became Professor of Bacteriology and Histology in the University of Denver Dental College in 1898. He graduated in medicine from Denver and Gross College of Medicine in 1903, and worked in the Departments of Laryngology and Otology of the University of Colorado School of Medicine from 1905 to 1936. President of local medical and dental societies early in his career, he became the first president of the Colorado Otolaryngological Society and of the Colorado Society for Crippled Children. A reserve medical officer since 1914, he was a major in the Medical Corps, United States Army, in 1918 and 1919.

In the national field, he became one of the original members of the American Board of Otolaryngology. His meticulous care in the examination of candidates will be remembered by all. His accurate and thorough presentations before the great special societies brought him the following presidencies: American Academy of Ophthalmology and Otolaryngology, 1923; American Laryngological, Rhinological and Otological Society, 1936; American Laryngological Association, 1941; and Chairman of the Section on Otolaryngology of the American Medical Association, 1931. He was an honorary member of the Pacific Coast Oto-Ophthalmological Society, and of the Texas Ophthalmological and Otolaryngological Society, the Kansas City Ear, Nose and Throat Society, and the Illinois State Medical Society.

He was a member also of the American Otological Society, of the American Society of Oral and Plastic Surgeons, the American College of Surgeons, the American College of Dentists, and the International College of Surgeons.

Numerous contributions on diseases of the mouth, nose, throat and ears, and on the development of the facial bones attested his skill as a surgeon and a teacher, and he wrote notable sections in the Jackson-Coates system of 1929 and the Jackson-Jackson text of 1945. He presented an authoritative paper on the development of the nasal accessory sinuses at the International Congress of 1928 in Copenhagen. His graduate teaching in the Denver summer courses was outstanding, and he was always ready to appear before such gatherings, with excellent slides and motion pictures. His health had failed after an appearance at such a meeting in Texas late in 1945; but he was in attendance at the Chicago meetings of the national societies in May of 1946, although relieved of the difficult tasks of the Board of Otolaryngology at that session.

Mrs. Carmody, the former Miss Mary Jane McBride, a Michigan girl whom he had married in Denver in 1899, was his constant companion and helpmate at these meetings. They have two married daughters and a son. Their great pleasure together has been travel and photography, notably of the romantic and colorful Southwest. But, on his last short flight from Denver to a meeting in Pueblo, Colorado, Mrs. Carmody was not with him. At 71, Tom Carmody went to sleep forever, in his seat aboard the plane.

His position in American otolaryngology, as a master in his combined field, is unique and secure. His colleagues on the Board and in the societies which he led deeply regret his passing, and would uphold his example of studious devotion to high ideals of medical education, as well as to the interests of deformed and underprivileged children.

RALPH A. FENTON.

Abstracts of Current Articles

EAR

Experimental Histological Studies on the Labyrinth.

Mygind, S. H. and Falbe-Hansen, J.: Acta Oto-laryngologica 34:59, 1946.

Studies of the labyrinth of experimental animals after the intravenous injection of histamine showed vasoconstriction. After the injection of adrenalin there was vasodilatation, presumed to be a compensatory reaction to changes in blood pressure. Slight hemorrhages in the choroid plexus were noted after injection of adrenalin while marked hemorrhages everywhere outside the labyrinth followed the injection of histamine. The water-binding power of the labyrinthine cells is increased by histamine, lowered by adrenalin.

HILL.

Treatment of Hardness of Hearing and Tinnitus with Vitamin B.

Johansen, H.: Acta Oto-laryngologica 34:176, 1946.

Twenty-four patients with long-standing partial nerve deafness and seven patients with otosclerosis were treated with vitamin B. No patient showed improvement of hearing. Three of 12 patients suffering from tinnitus were relieved of this symptom and remained so for six months after conclusion of treatment. While realizing that any such relief might be largely psychological, the author feels it should be given a trial when other methods fail.

HILL.

Psychogenic Deafness.

Truex, E. H., Jr.: Connecticut State M. J. 10:907-915 (Nov.) 1946.

Studies of 4000 soldiers with impaired hearing revealed that the hearing loss was functional in part or entirely in one out of every 12 and probably there were others in which the functional element was not recognized. Minor degrees of functional loss and functional elaboration of organic hearing loss were more frequently encountered than total hysterical deafness.

Functional hearing loss may be called the capacity to "not listen." When introduced as a part of a mental or emotional turmoil the hearing loss is measurable. The author feels that this condition is not uncommon in civilian life, although it is usually not recognized, and that a few of the successes and some of failures of the fenestration operation may be attributed either to the power or the impotency of suggestion.

Diagnosis is difficult and depends upon many observations. Inconsistencies in the history and the functional test are suggestive, especially a large discrepancy between loss for speech and for the pure tone speech range. Tests of labyrinthine function are of substantiating value in cases in which there is apparent severe auditory damage. By establishing the threshold for speech and for static noise and increasing the latter as a masking device, it was found that the patient with a functional impairment had his hearing for speech masked before the noise reached the intensity level previously established.

Treatment is psychiatric, frequently under barbiturate narcosynthesis, but suggestions and encouragement from the otologist are helpful.

HILL.

A Study of the Deafness in Meningococcal Meningitis Treated with Sulfonamides.

Tello, A.: Rev. De Otorrinolaring. 6:33-49 (June) 1946.

In the winter of 1941-1942, there occurred in Chile an epidemic of meningococcal meningitis. The author gives a résumé of his experiences with lesions of the labyrinth which were encountered and of the investigations which led him to formulate a new conception of the pathology and treatment of this disease.

A total of 1068 cases were studied. Neurolabyrinthitis developed in 32 cases. Of these patients, 22 sustained complete loss of hearing and 10 recovered with partial hearing. In these 10 patients, however, there was complete loss of vestibular function. Bearing in mind the dictum that the most primitive structures have the greatest resistance to disease, the author sought an explanation of why the labyrinth suffered more damage than the cochlea.

A comparative study of the perilymph in fatal cases of all types of meningitis was begun. In all of them he found that the perilymph shared equally with the spinal fluid in its reaction to infection. This

was demonstrated by the production of globulins. Such a finding is contrary to the teaching of Rius, who has stated that the perilymphatic space functions as a prospective filter against the progress of infection. It coincides and gives clinical significance to the work of Yampolsky, who injected china ink into the lumbar subarachnoid space of living dogs and cats and demonstrated its presence in the perilymph.

A very important role is claimed for cerebrospinal hypertension, which is induced by the infection and altered chemical reactions of the fluid. Although the infection itself is capable of destroying both the vestibular and cochlear functions, the question arises as to why there was, in 10 cases, partial cochlear recovery and complete loss of vestibular function. This condition developed while the patients were receiving intensive sulfonamide therapy which completely checked the disease.

The author finds a satisfactory explanation in the difference between the anatomical structures of the vestibular and cochlear perilymphatic spaces. In the vestibular portion there is a fine mesh of connective tissue trabeculae between the osseous and membranous labyrinths which obstructs the free flow of the perilymph. This fine trabecular structure is entirely absent in the cochlear portion and the flow of perilymph is unimpeded. Excessive pressure in the cochlear portion could quickly be reduced to normal by equalization through the scalae. In the vestibular portion, the obstruction is sufficient to delay any reduction of pressure and irreparable damage is inflicted upon the end organs.

If this theory is correct, it is an indication for a treatment originated by Riley to reduce cerebrospinal hypertension. This consists of non-liquid diet, intravenous dextrose, frequent spinal puncture and daily catharsis by magnesium sulphate. The author was able to try this treatment in only two cases. He expresses his satisfaction with it and his hope that it will be given further trial.

HIGBEE.

Studies on the Effect Upon the Hearing Through Air Conduction Brought about by Variations of the Pressure in the Auditory Meatus.

Rasmussen, H.: Acta Oto-laryngologica 34:415-424, 1946.

The effect of increasing and decreasing the pressure in the external auditory meatus upon hearing was studied in normal subjects.

At the lower frequencies the intensity of the sound was greatest at zero and decreased by increased or lowered pressure. Findings were uncertain for the middle frequencies. For the higher frequencies, 8200 and 11,600 c.p.s., the intensity of the sound was increased at a pressure of 30-50 cm. of water. The most likely explanation of this finding is an increased intralabyrinthine pressure caused by the stapes being forced into the fenestra ovalis. This is in line with Hughson's experiments with grafts applied to the round window.

HILL.

On the Treatment of Purulent Otitis Interna with Sulfonamides.

Sürala, U.: Acta Oto-laryngologica 34:200, 1946.

Based upon the observation of four cases the author concludes that with adequate sulfonamide therapy and an operation on the mastoid, labyrinthectomy may be postponed and frequently avoided under conditions which formerly would have made operative intervention in the internal ear imperative.

HILL.

The Course of Otitic Facial Palsy Under Adequate Treatment of the Disease of the Ear.

Kettel, K.: Acta Oto-laryngologica 34:311-316, 1946.

This paper is based upon the observations on 264 cases seen over a period of 30 years. The author does not feel that a negative faradic response is an indication for operative interference. Preoperative palsy in acute otitis media usually requires only adequate treatment of the ear condition. Decompression is done when, after mastoidectomy, there is no sign of returning motion after two months.

If during a radical mastoidectomy a fistula is discovered on the facial canal, decompression is done simultaneously; otherwise the patient is observed for two months. Facial paralysis occurring in conjunction with the operation indicates immediate decompression and repair of the nerve. Postoperative palsy occurring after a free interval has a good prognosis and decompression is only considered after two months' observation without signs of returning motion.

HILL.

NOSE

Osteomyelitis of the Sphenoid.

Morales, E.: Rev. De Otorrinolaring. 6:1-8 (March) 1946.

The difficulties of a clinician, confronted by a rare and serious illness and working under the handicap of inadequate resources for investigation, are related with admirable candor.

A case of osteomyelitis of the sphenoid bone in a boy 14 years of age is reported. The history covers a period of two and one-half years, during which time the diagnosis remained uncertain. The treatment and the efforts to determine the real basis of a perplexing illness are described.

In February 1943, the patient developed a fever of 40° C. and pain in the left ear and left side of face. The following day, a left peritonsillar abscess was incised. Only a few drops of pus drained from the incision.

There followed in succession an inflammatory edema of the left half of the head and neck, meningismus, and papillary edema. Thrombophlebitis of the cavernous sinus, left lateral sinus, and internal jugular vein was thought to be developing from the peritonsillar abscess.

Sulfonamides were given in doses of eight grams a day for ten days. The temperature became normal, the meningismus subsided, and the patient was greatly improved generally except for a mass over the left parotid gland. This was considered to be an abscess which was incised, but no pus was found. Following the incision, there was facial paralysis and a salivary fistula.

In May, three months after the initial symptoms, there was a generalized epileptiform seizure with loss of consciousness. Neurological and x-ray examinations failed to give additional information.

During September, seven months after the initial illness, the edema of the head, face, and neck recurred, and, for the first time, exophthalmus was present. The administration of sulfonamides again reduced the edema.

Consultations were held by the author with a number of his colleagues, but no satisfactory diagnosis was made. A tonsillectomy was performed. Shortly after this, a spontaneous fistula developed with pus draining from the external angle of the left orbit. The culture was reported as staphylococcus aureus.

During the ninth month of the disease, there was a third acute episode characterized by edema and pain localized in the right temporal area. This area was incised but no abscess was found.

At this stage of the illness, there were temporal edema, exophthalmus, orbital fistula, parotid fistula, and facial paralysis, all on the left side. On the right side there was temporal edema; when this area was incised, it showed periostitis without abscess.

In the seventeenth month of the disease, the patient noted small hard pieces, very like bone, in the discharge from his nose. Examination convinced the author that they were pieces of bony sequestra. After additional consultation and further x-ray studies, which the author states were not correctly interpreted, a radical operation was performed on the right maxillary and ethmoid sinuses. No pathological condition was discovered during this operation.

Two more acute phases of the chronic infection developed in the following year. They were controlled by penicillin.

Finally, at the end of two and one-half years, the author took the patient to Santiago, where the diagnosis of osteomyelitis of the sphenoid was made. The diseased bone was not accessible for surgery and massive doses of penicillin were recommended. Five million units were given in doses of 30,000 units every four hours. The edema and exophthalmus remained uninfluenced by this therapy.

The author then injected 10,000 units of penicillin daily into the areas of the temporal edema and the orbit, back as far as the sphenoid. This gave the only relief manifested during a period of three years. At the time of reporting this case, the exophthalmus had greatly subsided and the general condition of the patient was so much improved that a complete recovery was predicted.

HIGBEE.

Perforatio Septi Nasi - Free Transplantation.

Behrman, W.: Acta Oto-laryngologica 34:78, 1946.

The author suggests the use of fascia lata to close perforations of the nasal septum. The septum is radically resected and the transplant, taken from the thigh, inserted and anchored with catgut. The nose is then packed with gauze saturated with sulfathiazole suspension which is left in place for one week. Three cases are reported.

HILL.

On Phagedenic Ulcers in the Nasal Area.

Siirala, U.: Acta Oto-laryngologica 34:365-378, 1946.

This paper covers the clinical picture, pathology, bacteriology, diagnosis, treatment, and prognosis of phagedenic ulcers of the nose. Three cases, all fatal, are reported. The author objects to the term malignant granuloma as this would seem to denote a proliferative process. Actually the lesion is a gangrenous ulcer which is destructive of tissue and against which the organism is not capable of a productive defense.

HILL.

The Bacteriology of Maxillary Sinusitis.

Sparrevohn, U. R., and Buck, A.: Acta Oto-laryngologica 34:425-435, 1946.

Bacteriological studies on secretions taken from punctures of the inferior meatus showed a predominance of pneumococci in acute cases and hemolytic streptococci in chronic cases. Mixed infections were found chiefly after repeated punctures. The clinical course of sinusitis was found shortest in patients with sterile secretions, and longest in those with hemolytic streptococci.

HILL.

PHARYNX

Roentgenography of Adenoids.

Weitz, Harry L.: Radiology 47:66-70 (July) 1946.

A single lateral roentgenogram of the pharyngeal area gives much anatomical and pathological information. Factors used and positioning of patient's head are described. Advantages of x-ray over clinical examination of the nasopharyngeal area are: (1) the examination is simple, (2) the degree of breathing space encroachment can be accurately determined.

JORSTAD.

LARYNX

The Results of Laryngectomies Performed During the Period From 1928 to 1945.

Thornval, A.: Acta Oto-laryngologica 34:331-338, 1946.

Eleven cases are reported. Only three patients survived more than one year. All had advanced cases of cancer and were poor operative risks. The great majority of laryngeal cancers were treated

by the Coutard method or roentgen therapy. In the type of case referred to, the author prefers a two-stage technique, the first stage being the formation of the tracheal stoma. This is completed in its final form, not being merely a preliminary tracheotomy. Local anesthesia was used in all cases.

HILL.

ESOPHAGUS

Regarding Certain Methods of Facilitating Local Therapy and Prognosis in the Care of Oesophageal Strictures.

Skoog, T.: Acta Oto-laryngologica 31:78, 1943.

Discussing the management of lye strictures the author advocates early esophagoscopy under intratracheal anesthesia. At this stage there will not be the difficulties of irregular cicatrices found later and the risk of perforation can be lessened by the use of a general anesthetic. Treatment is instituted about the eighth day by the insertion of a Dauer sound to effect calibration of the lumen. In case of old neglected cicatrices he advises the diathermic removal of transverse adhesions which may prevent dilatation.

HILL.

MISCELLANEOUS

Chronic Toxicity of N'pyridyl, N'benzyl, Dimethyl-Ethylenediamine Monohydrochloride (Pyribenzamine).

Koepf, G. F., Arbesman, C. E., and Munafo, C.: J. Allergy 17:271-274 (Sept.) 1946.

The authors of this paper have rather accurately determined what, if any, toxic reactions were manifested in dogs that were given pyribenzamine daily over a period of a year. They used five basset hounds and two of the dogs were given 100 mg. daily; two more were given 200 mg. daily; the remaining dog was not given any pyribenzamine.

They found that through the twelve-month period the dogs remained in good health and exhibited normal activity. There was no evidence of kidney disfunction, no abnormalities of liver function, no instances of granulocytopenia or other damage to the hemopoietic system.

As the result of these observations, they then selected three healthy male subjects, 22, 23, and 24 years of age, respectively, and each of these subjects was given 150 mg. of pyribenzamine daily for eighty days. Routine examinations were made and there was no alteration in the general state of well-being, body weight, or blood pressure. There were also routine examinations made of the urine and no abnormalities were detected. Liver function, as indicated by icteric index, serum bilirubin, albumin, globin, prothrombin time and the cephalin flocculation tests, remained normal.

The authors admit, however, that such limited studies in man are not sufficient to attest to the complete harmlessness of the drug.

McLAURIN.

Clinical Studies with N'pyridyl, N'benzyl, Dimethyl-Ethylenediamine Monohydrochloride (Pyribenzamine).

Arbesman, C. A., Koepf, G. F., and Lenzner, A. R.: J. Allergy 17:275-283 (Sept.) 1946.

The authors of this paper made their observations after a study of 495 patients chosen from private practice, the Allergy Clinic of the Buffalo General Hospital, and the Allergy Clinic of the Children's Hospital of Buffalo.

They started out on the assumption that the report of Lewis in 1927, postulating the existence of a histamine-like substance, designated by him as H-substance, is liberated by the tissues at the site of the allergic reaction. Many investigators later came to the belief that H-substance was very closely allied to histamine and that it was reasonable to assume that any antihistaminic drug serving as an H-substance antagonist might prevent or attenuate many allergic reactions.

In their study of the 495 patients, the effective dose of pyribenzamine varied greatly in the individual case, depending to a marked extent upon the allergic state that existed and the degree of exposure to the offending allergens. The average adult dose, however, was from 100 to 400 mg. daily and from 50 to 200 mg. for children. In a few instances, as much as 1200 mg. were given to an adult in 24 hours without any serious untoward effects. It was always given orally and usually in four daily divided doses.

There were a few side reactions from pyribenzamine and the most common one was sedation though in some instances there was

dizziness, faintness, headache, fatigue, or an "all gone feeling." A smaller number of patients complained of excitability, palpitation and insomnia. The commonest gastro-intestinal disturbance was nausea, occasionally associated with vomiting. A few women complained of early menses while taking pyribenzamine. It was also noted that patients who received the larger doses of the drug were more likely to have side reactions than those receiving smaller doses, and that in these instances the dose could be reduced and still be effective. Where drowsiness was a disturbing side reaction it was controllable to a marked extent by having the patient drink strong coffee shortly after taking the drug.

The observations on the general effect of taking pyribenzamine was that it relieved itching of the skin and reduced the urticarial wheals. It also gave considerable relief to the itching of eyes, rhinorrhea, nasal blockage, and in some instances it relaxed bronchial spasm where asthma was present.

They concluded that it was advisable to give the drug to a known allergic patient prior to that patient's exposure to the allergen and in such event the allergic reaction would be prevented. These authors summarize their paper as follows:

"1. Clinical studies with pyribenzamine were done on 495 patients, having a total of 565 allergic manifestations.

"2. Pyribenzamine relieved sneezing, rhinorrhea, and nasal occlusion in 75 per cent of 313 patients with allergic rhinitis.

"3. Pyribenzamine relieved or prevented dyspnea, and cough in 48 per cent of the 98 patients with bronchial asthma.

"4. It relieved the pruritus and lessened the degree of erythema and wheal formation in 83 per cent of the 154 patients with urticaria.

"5. Pyribenzamine is apparently harmless in effective doses. It has some undesirable, although not serious, side effects."

McLAURIN.

Histamine In Rhinitis

McLaurin, J. W.: Laryngoscope 56:253-281 (June) 1946.

McLaurin reports his favorable experiences in the use of histamine azoprotein (hapomine) in a wide variety of cases all having an allergy basis. Included in the group were 40 cases of vertigo, 9 of

periodic headaches, 41 cases of vasomotor rhinitis and 12 of aural dermatitis.

The initial dose is .05 cc. The second dose is 0.1 cc., and each succeeding injection is increased by 0.1 cc. until a dosage of 1 cc. is reached. The injections are usually given on alternate days, unless symptoms are particularly distressing, when they are given daily, and in dermatitis cases, have been given twice daily. After the level of 1 cc. is reached, injections in this dosage are given weekly for four doses, and are followed by maintenance doses of 0.5 cc. weekly for eight weeks.

The usual patient receives a total of 9.55 cc. of histamine azoprotein over a period of approximately 13 weeks. In the occasional case a larger dose over a longer period of time is required, and in a few instances maintenance doses have been taken for a year or more. In a few cases results have been so prompt that treatment was discontinued short of the usual level.

All patients treated with histamine azoprotein, without exception, are required to remain in the office under observation for a minimum of 20 minutes after each injection. During this time a syringe of epinephrine, the specific physiologic antagonist to histamine, is kept at hand, although only occasionally has it been necessary to use it.

McLaurin's favorable experience with this method suggests a more extended trial of desensitization by histamine, particularly in the form of histamine-azoprotein, in so-called "intrinsic" allergy.

VAN ALYEA.

Clinical Experiences with a New Antihistaminic Drug.

Eyermann, Charles H.: Journal of Allergy, July, 1946.

Dr. Eyermann is reporting on the use of B-dimethylaminoethyl benzhydrl ether hydrochloride in the treatment of 52 cases of pollinotic vasomotor rhinitis. He states that this synthesized drug is of low toxicity and belongs to the pharmacologic group having the property of preventing some of the effects of histamine. Dr. Eyermann calls attention to the work of Loew, Kaiser, and Moore who showed that this drug alleviated the symptoms and diminished the mortality in guinea pigs when histamine was administered to the pigs as a mist or intravenously.

The results that the author obtained in the treatment of his 52 cases of pollinotic vasomotor rhinitis were classified as helpful when all symptoms were ameliorated, as questionably helpful when some of the discomfort was ameliorated, and as a failure when all of the discomforts of the vasomotor rhinitis persisted in spite of the administration of the drug. He found the drug helpful in 35 cases (67 per cent), questionably helpful in 12 cases (23 per cent), and a failure in 5 cases (9 per cent) of the cases studied.

He had instructed his patients to take 50 mg. of the drug at that period of each 24 hours when the patient expected the greatest degree of discomfort and to take further doses of 50 mg. at intervals of four to eight hours as needed for the relief of symptoms. Of 35 patients who had satisfactory relief, 5 obtained results by the use of one 50 mg. capsule in each 24 hours; 14 of them required 50 mg. of the drug night and morning; the remaining 16 of the patients required 50 mg. at intervals of four to eight hours. Some of these patients required an increased dosage with the advancing season and then decreased the dosage as the symptoms disappeared or as the season waned. It was noted that during an acute episode, the patients showed improvement in from twenty to thirty minutes after taking the drug and in several instances it was observed that the bleary, streaming eyes, nasal blockage and coryza, and other attendant ancillary discomforts changed to complete comfort in 20 minutes after 50 mg. of the drug was given. The drug was never taken when the symptoms were absent. The degree of relief, the size dose required to give such relief, or the length of time during which the drug would have to be administered could not be determined by the history of the case as regards its duration, the degree of sensitivity, the influence of hyposensitization injections, or sex.

In the 12 cases where the drug had questionable value because all symptoms were not ameliorated, there was control of sneezing in 7 of these cases but there was no relief of nasal blocking. In 4 of the cases there was less sneezing and nasal blocking with the development of chest oppression or wheezing while taking the drug. In one case there was relief from the sneezing and blocking for only two days. In 6 of this group there was a purulent nasal discharge.

In the 5 unbenefited cases classified as failure, all of the persons were women, ranging in age from 17 to 45 years, and all were sensitive to 10 protein nitrogen units per cubic centimeter of ragweed; 4 out of the 5 were sensitive to other allergens than ragweed alone. Of these patients, 4 also had a purulent nasal discharge.

The principal side reactions of the drug have been mentioned by Dr. Eyermann, and he saw these symptoms in 20 of his cases. There was somnolence in 10 instances; "dry" nose in 5; vertigo in 3; nausea in 2; weakness and nervousness in 2 instances each; palpitation, insomnia, and abdominal cramping in one instance each. In a few of these cases, these disagreeable symptoms disappeared when the dosage was reduced but reappeared when the dosage was increased again. In all instances, the side reactions became less troublesome when the drug was continued in the same dosage.

Dr. Eyermann also calls attention to 14 cases of chronic urticaria with the duration varying from two months to fifty years. In 7 of these cases the cause had been undetermined; 3 were classified as estrogenic urticaria; one was due to aspirin; one to hypothyroidism; one to focal infection; and one to insect bites (duration one week). The drug relieved the itching in from 20 to 30 minutes coincident with gradual subsidence of the whealing, though the erythema persisted for several hours after the drug had been used. In 9 of the cases, the urticaria was controlled with 50 mg. of the drug given once or twice a day. In 3 of the cases 150 mg. to 250 mg. had to be administered every 24 hours to maintain the same degree of comfort that had first been obtained by administration of only 50 mg. of the drug in the 24-hour period. This indicated definitely the necessity of increasing the dosage of the drug to maintain the same effect and was indicative of a tolerance that was gradually developed to the drug.

Among other very interesting points that Dr. Eyermann determined is that in cases of perennial vasomotor rhinitis there were some patients who were relieved of all of their symptoms while the drug was being used, but the symptoms promptly recurred when the drug was stopped. He also found that primary nasal polyposis, vernal conjunctivitis, dysmenorrhea and migraine were not satisfactorily influenced by the drug.

McLAURIN.

Histamine Antagonists. II Summary of Developments in Nonspecific Inhibition of Histamine, Anaphylaxis, and Allergy.

Feinberg, Samuel M.: Journal of Allergy, July, 1946.

The author of this paper reviews the work that has been done over a period of many years to determine the exact relationship of histamine to anaphylactic reactions and the effect of various histamine antagonists on such reactions.

Dr. Feinberg reminds us of the fact that the role of histamine in anaphylaxis has been the object of study and discussion since Dale and Laidlaw, in 1911, claimed that the injection of histamine into animals caused the toxic symptoms of anaphylactic shock. Lewis showed that there was a triple response in man, displayed after injury to the skin by physical, thermal, chemical, or allergenic agents and that it was identical with the local manifestations produced by the intracutaneous injection of histamine. The origin of histamine was conclusively demonstrated by Best and his co-workers who showed it to be a normal constituent of many tissues.

The author calls attention to two compounds, Pyribenzamine and Benadryl, which are now receiving the greatest attention on the part of the general medical profession and also the public. He states that they represent the best antihistamine agents that have been developed to the present time. Benadryl is effective in essentially all cases of urticaria factitia and dermographism and is especially helpful in the type of dermographism that frequently interferes with cutaneous testing for atopic reactions. He is in agreement with Friedlaender when he states that the drug is almost without beneficial effect in controlling allergic rhinitis or asthma. It was thought possible, therefore, that the topical application (nasal) in such cases might be effective. It was found, however, that even 0.5 per cent solution is locally irritating.

The author then concludes his paper by some very worthwhile statements regarding the use of such drugs. He reminds us that where the drug proves to be of benefit, it is important that we realize the drug must be considered palliative only. It may temporarily correct the result of the antigen-antibody reaction in the tissues but surely cannot be considered as curative. Furthermore, there are certain toxic actions of these drugs that must be anticipated. The most frequent unsatisfactory side effect of Benadryl is sleepiness and lassitude, but this symptom is not serious and does not even preclude the use of larger doses of the drug unless the symptom interferes considerably with the occupational demands of the patient. He also warns us of the possibility in individual instances of remote toxic effects on the hematopoietic and nervous systems.

McLAURIN.

Surgical Management of Infectious Asthma.

Woodward, F. D.: J. Allergy 17:260-264 (Sept.) 1946.

Dr. Woodward emphasizs the importance of allergists' being trained in otolaryngologic diagnosis and the progress that has been made by the otolaryngologist in clearing up sinus infections. Conversely, he states that the otolaryngologist should be well trained in allergic diagnosis and the methods available to the allergist in clearing up or controlling allergic reactions.

The author describes the general principal of examination that any otolaryngologist should make to determine the exact degree of involvement of the sinuses and especially calls attention to the importance of careful bacteriologic study. He also calls attention to the frequency with which the virus of a common cold activates a host of pathogenic pyogenic bacteria and advises that measures to create good ventilation to and from the sinuses be established early in the presence of an acute cold. He is under the impression that penicillin in sodium chloride solution, 500 units per cubic centimeter, used as a spray for the first few days is helpful in shortening the duration of the infectious process.

Dr. Woodward then describes the importance of lavage in helping to clear those sinuses that become acutely or subacutely involved. He states very definitely that a submucous resection of the nasal septum or resection of one or both middle turbinates, done under local anesthesia, gives excellent results when such procedures are indicated. He states he has never seen any harm in either of these procedures after having done them in several hundred cases.

The "complete operation" should not be considered too literally because it may eliminate all symptoms in bacterial sinusitis; whereas, in allergic sinusitis, because of a peculiar relationship of bacteria to pathologic changes, it may be absolutely impossible to call it complete since there may still be bone, scar tissue, regenerated membrane and bacteria present, which may act as a focus to stimulate the bronchial spasm. He thinks that this accounts frequently for the return of asthma in many cases. It is also his belief that it is definitely wrong to condemn surgery of the sinuses in asthma, because there are many procedures classified under this heading, from those that are ill-advised and poorly performed to those that are most carefully executed and complete. Those that may seem adequate at the time of operation may later prove to have been inadequate. He is convinced that one should not expect to cure asthma by surgery alone, but that an attempt to clear up a sinus infection by surgery is justi-

fiable regardless of whether asthma is existent in that case. Following that plan, it is possible to eliminate much pain by clearing up the sinus infection, restoring the airway, decreasing the discharge and toxemia, protecting the lungs from chronic changes, and eliminating a focus of infection. He feels that the clearing of the sinus infection may prove very valuable in helping to control the asthma in many instances.

Dr. Woodward makes the following statement in his conclusion: "Finally, I would like to say that I feel that otolaryngology has much to offer asthmatic patients, and that adequate sinus surgery should be employed whenever necessary, for our best results have been obtained by following this procedure in addition to allergic treatment."

McLAURIN.

Leucocyte Fragility in Transitory Leucopenia.

Squier, Theodore L.: Journal of Allergy, July, 1946.

Dr. Squier has called attention to transitory leucopenia as an important and characteristic finding in allergic reactions. He thinks that it is just as significant as eosinophilia and states that von Pirquet and Schick were of the opinion that in certain instances this leocopenia was the only recognizable manifestation of the allergy. According to Dr. Squier, the leucopenia is probably the result of a redistribution of leucocytes which occurs in allergic shock, and he is under the impression that the white cells are shunted into the lungs and possibly into the spleen and other organs when the anaphylactic reaction occurs. He calls attention to the significant finding of Webb, who showed that blood taken from the pulmonary vein of a dog in anaphylactic shock contained relatively few leucocytes as compared to the rather large number found in blood taken from the pulmonary arteries. By sectioning the lungs, enormous numbers of white cells were found crowding the capillaries and adherent to the vessel walls, thus confirming his impression that the leucopenia was the result of the additional number of white cells that crowded into the pulmonary area. He also calls attention to the fact that recently Abel and Schenck demonstrated a similar adherence of the leucocytes to the walls of the peripheral vessels. In the first phase of the allergic shock there was an arteriolar contraction with an obliteration of the lumen of the vessel. This was followed by an increased adherence of the white cells to the vascular endothelium and finally by migra-

tion of the leucocytes through the walls of the capillaries and the venules.

Although the redistribution of the leucocytes appears to be the finding of major importance, the author is under the impression that there is also an increased destruction of leucocytes in the presence of anaphylactic shock. However, leucocytolysis is actually much more difficult to demonstrate than erythrocytolysis because there is no pigment released on the destruction of the white cell that would serve as an index of its destruction; whereas, in erythrocytolysis there would be a demonstrable pigment indicating destruction of red cells.

In summarizing his paper, Dr. Squier makes the following statements:

"1. A method is described by which estimates can be made of white cell fragility roughly comparable to the estimation of red cell fragility in hypotonic saline.

"2. Evidence is presented to show that the transitory leucopenia seen following the ingestion of certain foods is accompanied by increased fragility of leucocytes.

"3. This increased fragility does not appear to be caused by a change in the relative proportions of the different types of white cells.

"4. It may well be the result of some alteration in the white cell membrane.

"5. No conclusion as to whether this change results from an antigen-antibody reaction or from chemical or mechanical trauma can be made from the present data."

McLAURIN.

On Osteomyelitis Frontalis Diffusa, with Special Attention to Its Relation to Sinusitis Frontalis.

Rojskjaer, C. E.: Acta Oto-laryngologica 34:445-477, 1946.

This is a rather extensive survey of the subject with the report of three cases, but with little or no reference to the influence of modern chemotherapy upon the clinical course of the diseases. The author states that penicillin had been hardly tested in Denmark although he did use sulfathiazole. The importance of early and radical operation is stressed.

HILL.

On Tumors of the Carotid Body.

Hamberger, C. A.: Acta Oto-laryngologica 34:104, 1946.

The differential diagnosis includes aneurysm, metastatic carcinoma, lymphoma, lymphosarcoma, tuberculous nodes, aberrant goitre, branchial cyst, neurofibroma. The clinical picture is usually that of a symmetrical, deep-seated, slowly-growing tumor at the level of the carotid bifurcation. This is movable only in the lateral plane. There may be pulsation which disappears on pressure of the carotid. There may be involvement of the vocal cord and occasionally contraction of the pupil on the affected side. The only treatment is surgical. To avoid irritation of the plexus caroticus with resulting heart stoppage it is suggested that a local anesthetic be injected in the region of the bifurcation, even in cases operated on under general anesthesia. Three cases are reported.

HILL.

Notices

GEORGETOWN UNIVERSITY

The Georgetown University Medical Center will sponsor an intensive graduate course in Oto-Rhino-Laryngology Bronchoscopy by Professor Georges Portmann, of the University of Bordeaux, France, for two weeks beginning April 7, 1947, at the Georgetown Medical School, Washington, D. C. Address inquiries to Dr. James A. Flynn, 1511 Rhode Island Avenue, N. W., Washington, D. C.

AMERICAN BOARD OF OTOLARYNGOLOGY

The American Board of Otolaryngology will conduct the following examinations in 1947: in St. Louis, Missouri, at the Coronado Hotel from April 16 to April 19; in Chicago, Illinois, at the Palmer House from October 7 to October 11. Communications should be addressed to the Secretary, Dr. Dean M. Lierle, University Hospital, Iowa City, Iowa.

BACK ISSUE OF THE ANNALS

The Annals is desirous of obtaining copies of the following issues now out of print: March 1940, June 1940, March 1943, June 1943, March 1944, June 1945, September 1945, and March 1946. $1.50 per copy will be paid for any of these issues returned to us. They should be sent with a memorandum of the sender's name and address to the Annals Publishing Company, 7200 Wydown Blvd., St. Louis 5, Missouri.

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OF THE

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American Broncho-Esophagological Association

President: Dr. Robert M. Lukens, 1001 Medical Arts Bldg., Philadelphia 2, Pa.
Secretary: Dr. Paul Holinger, 700 N. Michigan Ave., Chicago 11, Ill.
Meeting: St. Louis, Mo., Statler Hotel, April 22, 1947.

American Laryngological Association

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Meeting: Statler Hotel, St. Louis, Mo., April 23-24, 1947.

American Laryngological, Rhinological and Otological Society, Inc.

President: Dr. Harry W. Lyman, Carleton Bldg., St. Louis 1, Mo.
Secretary: Dr. C. Stewart Nash, 708 Medical Arts Bldg., Rochester 7, N. Y.
Meeting: Statler Hotel, St. Louis, Mo., April 25-26, 1947.

Sections:

Eastern—Chairman: Dr. Robert Ridpath, 1737 Chestnut St., Philadelphia 3, Pa.
Meeting: Philadelphia, Pa., January 13, 1947.
Southern—Chairman: Dr. Walter T. Hotchkiss, 541 Lincoln Rd., Miami Beach, Fla.
Meeting: Miami, Fla., January 6, 1947.
Middle—Chairman: Dr. Oliver E. Van Alyea, 135 S. LaSalle St., Chicago 3, Ill.
Meeting: Chicago, Ill., January 20, 1947.
Western—Chairman: Dr. Colby Hall, 1136 West 6th St., Los Angeles, Calif.
Meeting: Los Angeles, Calif., January 25-26, 1947.

American Medical Association, Section on Laryngology, Otology and Rhinology

Chairman: Dr. J. Mackenzie Brown, 1136 W. 6th St., Los Angeles 14, Calif.
Secretary: Dr. Fletcher D. Woodward, 104 E. Market St., Charlottesville, Va.
Meeting: Atlantic City, N. J., June 9-13, 1947.

American Otological Society

President: Dr. William E. Grove, 324 E. Wisconsin Ave., Milwaukee 2, Wis.
Secretary: Dr. Gordon D. Hoople, Medical Arts Bldg., Syracuse 3, N. Y.
Meeting: Statler Hotel, St. Louis, Mo., April 21-22, 1947.

ERRATUM

The meeting of the American Broncho-Esophagological Association will be held at Hotel Brighton, Atlantic City, June 9, 1947, and not in St. Louis on April 22 as printed on page 982.

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